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A cost comparison of introducing and delivering pneumococcal, rotavirus and human papillomavirus vaccines in Rwanda

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ABSTRACT

Background: Detailed cost evaluations of delivery of new vaccines such as pneumococcal conjugate, human papillomavirus (HPV), and rotavirus vaccines in low and middle-income countries are scarce. This paper differs from others by comparing the costs of introducing multiple vaccines in a single country and then assessing the financial and economic impact at the time and implications for the future. The objective of the analysis was to understand the introduction and delivery cost per dose or per child of the three new vaccines in Rwanda to inform domestic and external financial resource mobilization.
Methods: Start-up, recurrent, and capital costs from a government perspective were collected in 2012. Since pneumococcal conjugate and HPV vaccines had already been introduced, cost data for those vaccines were collected retrospectively while prospective (projected) costing was done for rotavirus vaccine.
Results: The financial unit cost per fully immunized child (or girl for HPV vaccine) of delivering 3 doses of each vaccine (without costs related to vaccine procurement) was $0.37 for rotavirus (RotaTeq®) vaccine, $0.54 for pneumococcal (Prevnar®) vaccine in pre-filled syringes, and $10.23 for HPV (Gardasil ®) vaccine. The financial delivery costs of Prevnar® and RotaTeq® were similar since both were delivered using existing health system infrastructure to deliver infant vaccines at health centers. The total financial cost of delivering Gardasil® was higher than those of the two infant vaccines due to greater resource requirements associated with creating a new vaccine delivery system in for a new target population of 12-year-old girls who have not previously been served by the existing routine infant immunization program.
Conclusion: The analysis indicates that service delivery strategies have an important influence on costs of introducing new vaccines and costs per girl reached with HPV vaccine are higher than the other two vaccines because of its delivery strategy. Documented information on financial commitments for new vaccines, particularly from government sources, is a useful input into country policy dialogue on sustainable financing and co-financing of new vaccines, as well as for policy decisions by donors such as Gavi, the Vaccine Alliance.

1. Introduction

Only a few detailed cost evaluations of the delivery of new vaccines such as pneumococcal, human papillomavirus (HPV), and rotavirus vaccines in low and middle-income countries exist [1–5]. This paper differs from other papers since it evaluates not only

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the costs of introducing individual vaccines, but also the costs of introducing multiple vaccines in a single country and then assesses the financial and economic impact at the time and implications for the future.

The policy implications of having accurate cost and financing information are several. These data can be used to improve planning of resource requirements and financing needs for multiple vaccine introductions at country level to evaluate their affordability. Understanding the delivery cost per dose or per child of new vaccines is important for informing domestic and external resource mobilization. Documented information on financial commitments for new vaccines, particularly from government sources, is a useful input into country policy dialogue on sustainable financing and co-financing of new vaccines, as well as for policy decisions by donors such as Gavi the Vaccine Alliance.

Rwanda is a small landlocked country with a population of 10.6 million located in East Africa. The Government of Rwanda (GOR) has had many achievements in health sector reform including the introduction of a system of performance-based financing and community-health insurance that covers more than 90 percent of the population with minimal co-payment. Rwanda has been very successful in achieving mortality reduction. Between 2005 and 2010, its child mortality decreased from 152 to 76 per 1000 live births and its infant mortality from 86 to 50 [6].

Rwanda was the first African country with national immunization programme introductions of pneumococcal conjugate vaccine (Prevnar®) in 2009, HPV vaccine (Gardasil®) in 2011 and rotavirus vaccine (RotaTeq®) in 2012. Prevnar® was initially provided in 2009 through Gavi via a donation from the manufacturer, Wyeth, and was then supported by Gavi with country co-financing beginning in 2010. [2] Gardasil® was provided through a three-year donation from the manufacturer, Merck, during 2011–2013 [7], and was supported by GAVI with country co-financing starting in 2014. Rotateq® was introduced in 2012 through Gavi support with country co-financing.

All three vaccines had the similar requirement of having 3-dose schedules for administration but the vaccine products differed in other aspects. The vaccine product presentations were different and this had consequences on the cold chain volume and waste management: Prevnar® was in a prefilled syringe for intramuscular injection (cold chain volume: 55.9 cm^3); RotaTeq® was in a single dose tube for oral administration (cold chain volume: 46.3 cm^3); and Gardasil® was in a single dose vial (cold chain volume: 15 cm^3) with separate syringe for intramuscular injection. Furthermore, target populations and delivery strategies for the three vaccines differed. Pneumococcal and rotavirus vaccines are recommended for infants and are commonly given through immunization sessions using the existing health system and existing health service delivery structure. The recommended target population for HPV vaccine is 9–13 year old girls [8], a population that has not been routinely served by immunization programs in most low or low middle income countries. Thus, the decision to introduce HPV vaccine in such countries requires creation of new vaccine delivery services in order to deliver multiple doses to each girl. In Rwanda, all three doses of HPV vaccine were delivered at schools to girls in primary grade 6 and were delivered at health facilities to a smaller proportion of girls (3%) who were not attending school.

The objective of the analysis was to estimate the cost of introducing and delivering each of the three vaccines nationwide in Rwanda, a low-income country, and to compare and understand the differences in cost components among the different vaccines to identify the main cost drivers.

Table 1
Description of vaccination activities in cost analysis.

	Description
Micro-planning	Meetings at national and district level for planning vaccine introduction activities
Training	Development of training curricula and materials, Training of trainers, training of supervisors, training of vaccinators at district/provincial level, training of monitors
Social Mobilization and Information, Education, and Communication (IEC)	Meetings with community leaders, IEC material development, production of leaflets, posters, TV spots, and radio, media/journalist workshop
Vaccine/injection supply procurement	Procurement of vaccines and injection supplies, clearance from customs, receiving, storage, and co-financing fees for Gavi supported vaccines
Service delivery	Personnel time spent on vaccination and traveling, per diem and transport costs associated with health worker vaccination of infants or adolescent girls.
Supervision, monitoring & evaluation	Supervisory trips by national and district-level program managers, production of registers and tally sheets, disease surveillance, and post-introduction evaluation
Waste management	Incineration and burial of syringes, safety boxes and vaccine containers
Cold chain	Purchase of additional cold chain equipment to store and transport vaccines

2. Methods

The analysis focused on estimating the incremental direct costs to the government health system of vaccinating children with the new vaccines and did not include existing costs of buildings or cold chain infrastructure. No indirect costs such as cost to the user (children, parents or caregivers) due to productivity losses were included.

The cost components for service delivery included startup costs (micro-planning, training, social mobilization and Information, Education, and Communication (IEC)), recurrent (vaccine and injection supply procurement, service delivery, supervision and monitoring and evaluation, and waste management) and capital costs (purchase of cold chain equipment). See Table 1 for a description of vaccination activities.

Both financial (or costs to the MoH) and economic costs were estimated so that opportunity costs could be compared. Financial costs included the value of resources purchased (or real expenditures) for the vaccine introduction. For example, these included resources used for vaccination (vaccines and injection supplies), training, social mobilization, transport and outreach allowances. Financial costs differ from economic costs since financial costs do not include resources that are already paid for or owned by the MoH such as the salaries of health personnel or resources paid for by external partners such as vaccines.

Table 2 provides an overview of the different cost components for calculating financial and economic costs. Service delivery is comprised of personnel, per diem and travel. However, salaries for personnel are already paid for by the Rwanda government, therefore, financial costs consist of per diem and travel allowances for personnel. These costs were only incurred for Gardasil since 97% of vaccines were delivered at schools, where health workers, community health workers and supervisors received per diem and travel allowance for the school based vaccination program. Rotateq and Prevnar were provided at health facilities.

[2] Rwanda switched its presentation of Prevnar® from prefilled syringe to vials (PCV13) when it switched to GAVI financing.

Table 2
Cost components by vaccine service delivery category.

	Financial	Economic
Startup		
Micro-planning	• Room rental • Refreshments	Financial costs plus the following: • Value of health worker time
Training	• Training materials • Supplies • Venue rental • Facilitator fees Per diems • Travel allowances	Financial costs plus the following: • Value of health worker time • For Gardasil also teacher or headmaster time
Social Mobilization/Information, Education, and Communication (IEC)	• IEC materials • Printing • Airing radio/TV spots • Venue rental • Material development meetings	Financial costs plus the following: • Value of health worker time • For Gardasil also teacher or headmaster time
Recurrent		
Service delivery	• Health worker per diems • Travel allowances • Fuel and maintenance	Financial costs plus the following: • Value of health worker time
Vaccine procurement	• For Prevnar and RotaTeq, there were Gavi co-financing costs but no costs related to receiving, customs clearance, or storage • For Gardasil which was a manufacturer's donation, no Gavi co-financing costs, but costs of syringes, receiving, customs clearance, and storage	Financial costs plus the following: • Cost of vaccines (less co-financing)
M&E, Supervision	• Fuel, per diem and travel allowances for supervisory trip • Printing new vaccination cards and tally sheets Post-introduction evaluation • Surveillance	Financial costs plus the following: • Value of supervisor time
Waste management	• Cost of waste disposal	Cost of waste disposal
Capital		
Cold chain equipment		Divided cold chain equipment purchase in 2007 between Prevnar and Gardasil. New refrigerators were purchased in 2011 for Rotateq.

Since vaccines were donated by Merck or obtained at subsidized prices by GAVI, the financial costs for vaccines included government co-pays to Gavi for Prevnar and RotaTeq, as well as financial outlays for receiving and storing vaccines at the airport and syringes for Gardasil. The government co-pays for Prevnar® or Rotateq® of $0.20 per dose were included as well as the cost of receiving and storing Gardasil®. Vaccine costs were not included as part of financial costs except for government co-pays to Gavi for Prevnar® and RotaTeq® since these commodities were donated; however, the government paid for receiving and storing the vaccines at the airport as well as to purchase syringes for Gardasil®. Service delivery financial costs (defined as per diem and travel allowances paid to health workers and supervisors and defined in Table 3) were only incurred for Gardasil® since 97% of this vaccine was provided at schools in Rwanda whereas the other two vaccines are provided at health facilities.

All three of the vaccines had three dose schedules but each had different sources of financing and prices per dose. Prevnar® was supported by Gavi through an Advance Market Commitment [11] and the price per dose was subsidized at $3.50 through this mechanism. Gardasil® was provided through a three-year donation from Merck and the country paid for syringes and receiving and storing the vaccine. We assumed that the price per dose of Gardasil® and RotaTeq® would be $5.00[3] per dose to the manufacturer and Gavi, respectively, for the economic costs.

The value of personnel time was included in the economic cost estimate. The time cost is estimated through multiplying the salary per minute by the number of minutes required for a vaccination. Additional outreach allowances are added for Gardasil vaccination since these activities took place outside of the health facilities.

The cost of additional cold chain equipment was depreciated[4] for each of the three vaccines. New cold chain equipment was purchased twice in preparation for the introduction of the three vaccines. The cost of new equipment was divided among the new vaccines.[5]

The financial and economic costs of all the resources used for vaccination were totaled and shown with and without the estimated cost of the vaccine so that service delivery costs could be analyzed. The total cost was also divided by the number of doses administered and number of fully immunized children (FIC) or girls (FIG) to estimate the cost per dose and cost per FIC/FIG. The year of analysis for each vaccine is the first full year for which the vaccine was introduced. Official exchange rates of the Rwandan Franc against the US dollar were used according to the year of actual or planned vaccine introduction (2010, 2011, or 2012) and were 580, 600 and 610 Rwandan francs per US dollar, respectively, and according to the Rwanda National Bank [12–14]. The reporting year is 2012 US$.

Since this analysis evaluated incremental costs, no shared health systems costs across the vaccines for sub-national vaccine supply chain logistics were included. Even though it was likely that some service delivery costs such as transport were likely to be incurred at the district and health facility level, these were not included due to lack of information. Thus, the total cost of delivering the vaccines was slightly underestimated.

[3] The assumption was made before GAVI negotiated a price of $4.50 for Gardasil with the manufacturer.

[4] The assumption for useful life years for cold chain equipment was 10 years for refrigerators with a discount rate of 3%.

[5] During the first cold chain expansion, new equipment were purchased in preparation for the introductions of Prevnar® and Rotateq®. After the Rotateq® introduction was delayed, the equipment purchased for this vaccine was instead used for the Gardasil® introduction. During the analysis, we divided the cost of the initial cold chain equipment between Prevnar® and Gardasil® and allocated the cost of the second set of equipment to Rotateq®.

Table 3
Assumptions made for delivery cost analysis of vaccines.

Vaccine	Prevnar®	Rotateq®	Gardasil®
Target population	376,202 infants 0-1 years in 2010	394,473 infants 0-1 years in 2012	91,317 girls in P6 in school (9-18 years) and 3,066 girls who were out of school and 12 years old
Number of doses per child	3	3	3
Price of Vaccine	Financial: $0.20 per dose co-financing Economic: $3.50/dose	Financial: $0.20 per dose co-financing Economic: $5.00/dose	Vaccines donated during 1st three years but MoH paid for syringes, receiving, clearance and storage; assumed $5.00/dose for economic costs (not inclusive of costs of receiving and storage of the vaccine)
Type of Vaccine, presentation and cold chain volume	Prevnar® in prefilled syringe for intramuscular injection, 55.9 cc	RotaTeq® in single dose applicator for oral administration, 46.3 cc	Gardasil® in single dose vial with separate syringe for intramuscular injection, 15 cc.
Administrative Vaccine Coverage	First dose coverage was reported to be 80%, then dropout of approximately 1% occurred for each of the 2nd and 3rd doses	Assume 80% coverage for 1st dose, with 1% and 0.5% dropout rates for 2nd and 3rd doses	First dose was reported to be 97% with dropout of 2% occurred for each of the 2nd and 3rd doses
Country Co-financing for Gavi	Rwanda began co-financing Prevnar®[a] in 2010 at $0.20/dose	Co-financing will begin in 2012 at $0.20/dose	NA
Introduction Costs (Micro-planning, training, Soc.Mob./IEC)	Assumed to last five years	Assumed to last five years	Assumed to last five years
Cold Chain	[b]Half of the cold chain equipment purchased for Prevnar was later used for HPV vaccines	New refrigerators were purchased for Rotateq®.for the district (87) and health center levels (131).	[b]Half of the cold chain equipment purchased for Prevnar was later used for HPV vaccines
Service delivery	Six minutes[c] vaccinator time per vaccination in clinic	Six minutes vaccinator time per vaccination in clinic	Six minutes[c] vaccinator time per vaccination in clinic Health worker outreach allowances (5000 Rwanda francs or approximately $8) for visiting each school; 2,510 schools were visited by teams of 2 health workers
Supervision	Supervisory trips three times a year: Travel allowance, per diem, fuel; staff salaries; 20% allocated to PCV	Supervisory trips three times a year: Travel allowance, per diem, fuel; staff salaries; 20% allocated to RV	Supervision takes place during HPV vaccination and included in cost of service delivery
Monitoring and evaluation	Printing of new vaccination cards and tally sheets, post-introduction evaluation, surveillance	Printing new vaccination cards, post-introduction evaluation, surveillance	Printing new vaccination cards, post-introduction evaluation, surveillance
Waste management	Incineration and Burial of prefilled syringes;	Incineration and Burial; Disposal of plastic dosing tubes	Incineration and Burial

[a] Rwanda obtained Prevnar as a donation from Wyeth, the manufacturer, in 2009 and the government only paid for transport, receiving and clearance; it began getting the vaccine through Gavi in 2010 and paying the co-financing fees.
[b] Since 50% of the cold chain costs for the Prevnar introduction were actually attributed to Gardasil introduction, the costs of introducing Prevnar was slightly underestimated.
[c] Based on program manager estimates.

Table 3 shows assumptions that were made in the analysis of costs to introduce the vaccines. The assumptions for vaccine coverage were based on the administrative coverage reported by Rwanda for Prevnar® and Gardasil®. We assumed that the same coverage for RotaTeq® would be achieved as for Prevnar.

2.1. Data collection

During January until May 2012, the study team, comprised of a Rwandan economist (CK), an international health economist (AL), and the Rwandan immunization program manager (MG), collected primary and secondary data on the costs of introducing the 3 vaccines using the WHO Cervical Cancer Prevention and Control Costing Tool (C4P) [9].

The WHO C4P Tool that was used for analysis was initially developed for estimating the cost of planned introduction of HPV vaccines in the United Republic of Tanzania [14]. The WHO C4P tool is an Excel based tool that enables the user to estimate and project the value of incremental (additional) resources required at national, provincial and district level to add the country-wide delivery of HPV vaccine to an existing immunization program over a five-year period. It uses a mixture of ingredients and expenditure approach to costing.

The WHO C4P tool was used to guide data collection and entry for the Gardasil HPV vaccine against cervical cancer. The tool was modified to estimate retrospective costs for Prevnar® and Gardasil®, as well as modified to estimate prospective (projected) costs of introducing Rotateq®. As Prevnar® and Gardasil® vaccines had already been introduced into the country at the time of this cost assessment, the cost analyses for those two vaccines were retrospective while for RotaTeq®, the estimated resource requirements of vaccination were projected.

Table 4 shows the data sources for the study. The study team collected data related to vaccine delivery on target populations, health facilities, schools, and costs and quantities of required resources from the national immunization program, Ministry of Education, the Ministry of Health (MoH), and the Rwandan Comprehensive Multi-Year Plan (cMYP) [10]. The team also interviewed immunization program managers and other partners (WHO, UNICEF, and USAID) to obtain information on programmatic options, cold chain equipment purchases and other cost data. They also collected data on facility and outreach costs from visits to a small sample of two health centers and one hospital. Note that since no data on waste

Table 4
Data sources for cost study.

Data	Sources	Type of data
Micro-planning, training, social mobilization/IEC, service delivery, waste management	Rwandan National Immunization Program, WHO	Primary/secondary
Number of health facilities	Rwandan Ministry of Health	Secondary
Number of girls enrolled in Primary 6 grade, number of schools	Rwandan Ministry of Education	Primary/secondary
Population size of infants and girls	Rwandan Bureau of Statistics	Primary/secondary
Health worker salaries	Rwandan comprehensive multi-year plan (cMYP)	Secondary
Cold chain expenditures	UNICEF, USAID, and Gavi	Secondary

management were available, the assumption was made that waste disposal cost $0.10 per vaccination.

3. Results of cost estimation of delivering Prevnar®, RotaTeq®, and Gardasil® Vaccines

Table 5 shows the total financial and economic costs of introducing and delivering the three vaccines, adjusted to 2012 US$ and the unit costs per dose of vaccine are found in Appendix 1. It should be noted that the total costs of introducing Prevnar® and RotaTeq® were affected by differences in the size of the birth cohort in 2010 and 2012 (376,202 and 394,473 infants, respectively).

3.1. Financial Costs

Total financial delivery costs were lowest for Prevnar® with an annual cost of $726,127. Costs were slightly higher for RotaTeq® (10%) and significantly higher for Gardasil® (51%). The largest cost component for Prevnar® and RotaTeq® was the vaccine co-financing, followed by monitoring and evaluation and supervision while the largest cost component for Gardasil® was service delivery due to the outreach allowances.

When startup costs were compared across vaccines, some variation was found. Training costs[6] were lower for RotaTeq® introduction than the other two vaccines since its training activities were combined with a larger training activity for multiple vaccines while Gardasil® vaccine introduction costs were higher due to greater social mobilization and training requirements. The substantial need for social mobilization and training was because the HPV vaccine was targeted to an older (non-infant) age group and only to girls and because vaccine delivery was primarily taking place in schools and school staff, in addition to health workers, required some training on the vaccine.

Recurrent costs were greater for Gardasil® than for the other two vaccines. The costs of introducing HPV vaccine were approximately 50% higher due to the additional service delivery costs of delivering the vaccine to a new target population in the absence of existing social mobilization and service delivery infrastructure for this population – in this case, vaccine delivery in schools. Recurrent costs were slightly higher for RotaTeq® than Prevnar® due to the larger infant target population in the introduction year (2012) than in the Prevnar® introduction year (2009/10). Waste management costs were lower for RotaTeq® since it was given orally and did not require disposal of syringes.

Table 5
Total financial and economic costs of three vaccine introductions in Rwanda in 2012 US$.

	Prevnar	RotaTeq	Gardasil
Target number of children to be vaccinated	**376,202**	**394,473**	**91,317**
Financial costs			
Startup			
Micro-planning	$4612	$4607	$13,197
Training	$23,959	$12,231	$44,283
Social Mobilization/Information, Education, and Communication (IEC)	$30,170	$30,170	$53,125
Sub-total	**$58,741**	**$47,008**	**$110,605**
Recurrent			
Service delivery	–	–	$735,009
Vaccines/injection supplies procurement	$565,366	$673,207	$156,503
Monitoring & evaluation (M&E), Supervision	$55,767	$61,902	$59,873
Waste management	$46,253	$4694	$36,139
Sub-total	**$667,386**	**$739,803**	**$987,524**
Capital: cold chain	–	–	–
Total	**$726,127**	**$786,812**	**$1,098,129**
Economic costs			
Startup			
Micro-planning	$59,543	$56,151	$84,146
Training	$111,412	$52,293	$107,628
Social Mobilization/IEC	$34,885	$34,885	$79,745
Sub-total	**$205,840**	**$178,214**	**$271,519**
Recurrent			
Service delivery	$243,662	$239,557	$904,918
Vaccines/injection supplies procurement	$4,471,911	$6,548,471	$1,951,594
M&E, Supervision	$83,541	$83,324	$82,057
Waste management	$59,161	$5,164	$48,672
Sub-total	**$4,858,275**	**$6,876,516**	**$2,987,241**
Capital: cold chain	$23,645	$32,895	$22,969
Total	**$5,087,760**	**$7,052,538**	**$3,281,720**

The unit costs of introducing the three vaccines are shown in Table 6 adjusted to 2012 US$. The financial unit FIC/FIG cost of delivering the 3 vaccines (without vaccine procurement costs) ranged from $0.37 for RotaTeq® to $10.23 for Gardasil® vaccine. The financial costs of Prevnar® and RotaTeq® vaccines were similar since both were delivered using existing health system infrastructure to deliver infant vaccines at health centers. The unit cost of delivering Gardasil® was higher than those of the two infant vaccines due to greater resource requirements associated with creating new vaccine delivery infrastructure to deliver vaccine to a new target population of 12 year old girls.

3.2. Economic costs

The largest share of economic costs was vaccine procurement for all three vaccines. When economic costs were compared for the three vaccines, the total annual costs were lower for Gardasil® vaccine than for the other two vaccines due to lower procurement costs – i.e., total procurement costs for Gardasil® were lower since its target population number of adolescent girls in Primary 6

[6] Training costs were projected based on plans specified by the immunization program manager.

Table 6
Financial and Economic Cost per Dose and Fully Immunized Child (FIC)/Fully Immunized Girl (FIG) of Introducing Three New Vaccines in Rwanda 2012US$.

	Prevnar in Syringe and Gavi Support	RotaTeq Vaccine with Gavi Support	Gardasil as Manufacturer Donation (no co-pay)
Financial costs			
Cost per dose (vaccine procurement costs + delivery costs)	$0.85		
	$0.84	$3.93	
Delivery cost per dose (no vaccine procurement costs)	$0.18	$0.12	$3.37
Cost per FIC/FIG (vaccine procurement costs + delivery costs)	$2.58	$2.53	$11.93
Delivery cost per FIC/FIG (no vaccine procurement costs)	$0.54	$0.37	$10.23
Economic costs			
Cost per dose (vaccine procurement costs + delivery costs)	$6.02	$7.51	$11.73
Delivery cost per dose (no vaccine procurement costs)	$0.68	$0.54	$4.76
Cost per FIC/FIG (vaccine procurement costs + delivery costs)	$18.16	$22.69	$35.66
Delivery cost per FIC/FIG (no vaccine procurement costs)	$2.08	$1.62	$14.45

grade was smaller than the total infant cohort of boys and girls for Prevnar® and RotaTeq®. The estimated cost of RotaTeq® procurement was greater than that of Prevnar® due to its higher price per dose.

Economic unit costs were also higher for Gardasil®. The cost of delivering the vaccine per fully immunized girl was $14.45 while costs per fully immunized child of delivering Prevnar® and RotaTeq® vaccines were $2.08 and $1.62, respectively. Economic unit costs with vaccine procurements were greater for RotaTeq® than Prevnar® due to RotaTeq®'s higher vaccine price. However unit costs of delivering RotaTeq® (without vaccine procurement) were slightly lower than for Prevnar® since RotaTeq® is administered orally, resulting in less waste management costs.

4. Discussion

The annual costs of delivering three new vaccines in Rwanda differed due to vaccine presentations, vaccine prices, and prior existence of health system for vaccine delivery or need to create new service delivery system for a new target population. Two of the vaccines, Prevnar® and RotaTeq®, are more easily integrated into the existing immunization program since these were targeted to children under one year old and delivered at health facilities while Gardasil® is targeted to an older age group and delivered in schools. The financial cost differences of introducing Prevnar® and RotaTeq® were small and could be attributed to vaccine presentation (also waste management requirements) while the variation in economic costs were more substantial due to a higher cost per dose for RotaTeq® than Prevnar®. Governments that are Gavi-eligible will have similar financial costs when introducing Prevnar® and RotaTeq® due to the same co-financing fees for procurement. However, if a government were not Gavi-eligible and were paying to procure the two vaccines,[7] there could be more significant differences in the cost of procuring the two vaccines.

The main financial cost differences between Gardasil® and the other two vaccines were due to delivery costs related to reaching a new target population and the reliance on delivering vaccines in schools. For Prevnar® and RotaTeq®, the largest share of financial non-vaccine costs was for supervision and monitoring and evaluation, while for Gardasil, it was for service delivery. The largest share of economic non-vaccine costs was service delivery for all three vaccines.

The largest economic cost component for all three vaccines was vaccines and injection supplies as was found in other studies [1–3]. However, the economic cost for vaccines and injection supplies was lower for Gardasil® since its target population includes only girls and was smaller than the infant cohort. The largest non-vaccine recurrent economic cost component was service delivery, which included transport, as found in other studies [1,2]. Another study [3] has found that cold chain expansion was the largest capital/startup costs and that startup costs accounted for the largest share of HPV vaccination costs [5]. This finding was similar to our findings that the largest non-annualized capital/startup cost for Rotateq® was cold chain. On the other hand, social mobilization was the largest capital/startup cost for the other two vaccines, Prevnar® and Gardasil® as in the study by Quentin and colleagues [1].

The main difference between the financial and economic cost analyses for startup costs is the inclusion of health personnel time; a substantial amount of health personnel time is involved in the startup costs of training, sensitization and service delivery in the introduction of Gardasil®. In planning for introduction of new vaccines, these personnel time costs need to be considered and taken into account since there is an opportunity cost to the health personnel time. Social mobilization and IEC activities are also particularly important to inform the population about the benefits of vaccination and how the vaccine will be delivered. Governments need to plan ahead for these operational costs since these will need to be financed adequately. Donors such as Gavi only partially finance the vaccine and do not fully support ongoing operational delivery costs. In addition, such advance planning allows human resources to be appropriately allocated and for the program to be successfully implemented.

The delivery strategy is particularly important to consider since delivery to a new target population that is currently without regular health services and which will be vaccinated outside health facilities requires more resources. Delivering Gardasil® was more costly since unlike new infant vaccines, delivery of Gardasil® was unable to piggy back on an existing routine immunization delivery infrastructure for the target population [15]. Instead, introduction of HPV vaccine required creation of a new routine vaccine delivery service for a new target population. The target population of 9–13 year old children usually receives limited or no routine preventive or other health services so there is limited or no existing preventive health service delivery system in place on which HPV vaccine delivery can depend. Delivering HPV vaccine three times within 6 months at schools in Rwanda required additional social mobilization and IEC, transport and per diems as well as additional health personnel time. Examination of the programmatic and cost differences between routine infant vaccine delivery and episodic delivery via campaigns has also been analyzed and taken into

[7] It should be noted that Rwanda introduced RotaTeq® vaccine. Another rotavirus vaccine, Rotarix® vaccine, has a 2 dose schedule (instead of RotaTeq's 3-dose schedule) and the 2012 Rotarix® cost per dose is more similar to Prevnar® If one were to compare costs of introducing Rotarix, the costs would be lower than those of introducing Prevnar®.

consideration for development of the Gavi introduction grant for HPV vaccines.

After the introduction year, some synergies were achieved through combining Gardasil® vaccination with delivery of other interventions and these could potentially be used to lower delivery costs. For example, HPV vaccination of girls was combined with delivery of deworming medication for delivery of one Gardasil® vaccine dose, thereby reducing the total amount of health personnel time required for this activity. In addition, Gardasil® vaccination for one dose in 2013 was combined with campaign delivery of measles-rubella vaccination; this reduced the costs of transportation and the total time spent by health personnel on these two immunization activities.

Limitations to this analysis should be noted which may have affected the accuracy of our cost estimations. Assumptions were made in the estimation of health personnel time spent on social mobilization and vaccination. Since the year of introduction in Rwanda for the three vaccines varied, mixed methods using primary and secondary data sources with both prospective and retrospective data collection had to be used. Due to lack of information, some service delivery costs such as cold chain maintenance and fuel at the district and health facility level, and energy to run the cold chain were missing. Thus, total costs of delivering the vaccines were underestimated. In addition, not including the shared health systems costs across the three vaccines such as shared personnel and cold chain rooms may have resulted in lower estimates. Another limitation of the analysis is that some district/health facility level costs were not included. Lastly, in this cost analysis, half of the actual cold chain costs for Prevnar® was attributed to Gardasil®, since by 2012 when Gardasil® was introduced, Rwanda had switched the pneumococcal vaccine it was using to a smaller vaccine product presentation; however, this analysis approach meant that the Prevnar® introduction costs were underestimated by 50% of the cold chain costs.

This analysis provides useful information for the Rwandan government to determine its financial outlays for new vaccines as well as opportunity costs for its personnel. It also provides important lessons for countries that are not Gavi-eligible or are graduating from Gavi support since it provides estimates of the economic costs that the government will have to pay for expenses such as vaccine procurement and cold chain equipment costs. A government will need to consider its ability to pay for these vaccines and for delivery costs, as such expenses have an impact on the sustainability of an immunization programme.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2015.10.022.

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