Breakeven Analysis for Various Human Papillomavirus Vaccine Presentations in Vietnam and Uganda

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Overview

Working in collaboration with the Vaccine Presentation and Packaging Advisory Group (VPPAG), representatives from the global health community are conducting a series of studies to guide presentation and packaging decisions for future human papillomavirus (HPV) vaccines targeted for low-income countries.[1] Presentation and packaging decisions, such as the number of doses per container, type of container, and recommended storage temperatures, greatly impact the way vaccines are handled, the quantity of vaccine wasted, and the ability of health workers to deliver the vaccines effectively and efficiently.

Based on input from countries, manufacturers, and global vaccine experts, the VPPAG has published a "generic Preferred Product Profile (gPPP) for vaccines." This document is intended to assist in aligning consumer demands with product design. By examining and communicating presentation and packaging preferences early in the development process, manufacturers of second-generation HPV vaccine can consider the specific needs of developing countries.

HPV vaccine presents unique characteristics that differentiate it from current World Health Organization (WHO) prequalified infant vaccines. HPV vaccine targets an older, gender-specific population; demands a higher price than most existing WHO prequalified vaccines; offers a promising thermostability profile; and is available as a liquid formulation without preservative. Thus, research is underway to generate additional evidence on the optimal formulation, doses per primary container, type of container, and storage conditions to supplement the gPPP for HPV vaccines.

The study highlighted in this report uses a breakeven cost analysis to compare potential prices, wastage rates, and cold chain requirements for various HPV vaccine presentations. This study employs an analytical tool developed by Andrew Garnett, PATH consultant, for the PATH Malaria Vaccine Initiative, entitled the Vaccine Presentation Assessment Tool (VPAT). The work to apply the tool to HPV vaccine data was supported by Project Optimize, a collaboration between the World Health Organization (WHO) and PATH with a unique mandate to create a vaccine supply chain that is flexible and robust enough to handle an increasingly large and costly portfolio of vaccines.

The VPAT compares the impact of introducing various presentations of an HPV vaccine given a country's existing portfolio of vaccines delivered and its supporting cold chain storage and transport infrastructure. Since national immunization programs and vaccine supply chain logistics are unique for each country, the results of the analyses that follow may only be applicable to the particular country assessed. In order to understand the extent to which these results can be extrapolated across low-income countries, a significantly larger sample of country analyses will need to be undertaken. However, the results that follow provide insight into key variables to consider when defining the attributes of future vaccines targeted to developing country markets.

Methodology

When the price of vaccine for one child represents 3% of the annual net income for the average person, minimizing the cost associated with delivery of the vaccine is important. To understand the impact that packaging and presentation have on the cost of vaccine delivery for a particular country, the VPAT applies variable costs and amortized capital costs associated with vaccine distribution from the point in which vaccine arrives at the central medical store to the point in which the vaccine is delivered to a child.

HPV vaccine manufacturers and the VPPAG are interested in comparing the cost to deliver vaccine in a single-dose vial, compact prefilled syringe, two-dose vial, and ten-dose vial. All presentations except the ten-dose vial are assumed to not contain preservative. For the compact prefilled syringe, two configurations are modeled based on the data from the Uniject® device (Uniject is a registered trademark of BD): one device packaged in a foil pouch ("individually packed") as well as 50 devices packaged in a re-sealable foil box ("multipack"). This report utilizes locally collected data from Vietnam and Uganda to model the impact that various HPV vaccine presentations have on vaccine supply chain volumes and costs.

Vaccine volume assumptions

Vaccines procured via the United Nations Children's Fund (UNICEF) are typically provided in a vial or prefilled injection device, referred to as the primary package, then inserted in a box or secondary package. Secondary packaging volume per dose assumptions for each of the presentations under consideration were determined using information collected from PATH, WHO, and vaccine producers (see Table 1). Volume per dose in the shipping container is calculated by multiplying the volume per dose of secondary packaging by the bulking or insulation factor. According to written correspondence from PATH's Vietnam office (October 2009) and from Uganda Expanded Program on Immunization (EPI) management staff (January 2010), vaccines shipped to Vietnam and Uganda do not require insulation in the shipping container, thus the bulking factor is minimal.

Table 1. Volume per dose assumptions for intermediate packaging[2]

Presentation options		Secondary packaging	Shipping container	Shipping container bulking factor	Comparable vaccine; source
		Vaccine (cm^3/dose)	Vaccine (cm^3/dose)		
Single-dose vial		15.00	18.75	1.25	Gardasil; R. Bielik, 2007[2]
Compact prefilled	Individual	24.60	30.75	1.25	HepB Uniject; BioFarma, 2009[2]
	Multipack	12.83	16.03	1.25	Uniject; Confidential, 2010
Two-dose vial		4.80	6.00	1.25	HepB; GlaxoSmithKline, 2009[2]
Ten-dose vial		2.50	3.13	1.25	Hib liquid; WHO, 2005[2]

Abbreviations/acronyms: HepB= hepatitis B; Hib= *Haemophilus influenzae* type b; WHO= World Health Organization.

In order to understand the true costs of introducing an HPV vaccine into a country's vaccine supply system, the estimated volume of existing vaccines, consumables, and wastes of the country's standard national immunization program is included in the analysis. For the purpose of this analysis, this is referred to as the "base" schedule. Volumes of existing vaccines were obtained from PATH country office personnel and included in the VPAT to determine the estimated volumes delivered per fully immunized person (FIP). The schedule of antigens and their respective characteristics for Vietnam and Uganda are listed in Tables 2 and 3, respectively.

Table 2. Base schedule and vaccine characteristics in Vietnam[a,3,4]

Vaccines in current schedule	Manufacturer (source)	No. of doses per FIP	Wastage rate (%)	Volume per dose (cm^3)[b]	Cost per dose ($US)
BCG 10d	IVAC	1	65%	11.41	0.061
DTP 20d	IVAC	3	35%	14.25	0.073
Measles 10d	Sanofi (UNICEF)	2	17%	21.15	0.293
OPV 20d	Poliovac	3	35%	5.54	0.050
TT 20d	IVAC	2	35%	10.89	0.033
HepB 2d	Vabiotec	3	5%	43.60	0.306
DTP-HepB+Hib 2d[c]	To be determined	3	5%	38.50	3.500

a. Data received via written correspondence from PATH's Vietnam office (October 2009).
b. Tertiary vaccine packaging; based on bulking factor of comparable WHO prequalified vaccines.
c. In 2010, Vietnam is expected to adopt pentavalent vaccine which will replace DTP and HepB vaccines.

Abbreviations/acronyms: FIP= fully immunized person; BCG= Bacilles Calmette-Guérin; d=dose; DTP= diphtheria-tetanus-pertussis; UNICEF= United Nations Children's Fund; OPV= oral polio vaccine; TT= tetanus toxoid; HepB= hepatitis B; DTP-HepB+Hib= liquid diphtheria-tetanus-pertussis-hepatitis B+lyophilized *Haemophilus influenzae* type b.

Table 3. Base schedule and vaccine characteristics in Uganda[5,6]

Vaccines in current schedule	Source	No. of doses per FIP	Wastage rate (%)[a]	Volume per dose (cm^3)[b]	Cost per dose ($US)[a]
BCG 20d	UNICEF	1	70%	7.65	0.105
TT 20d	UNICEF	1	20%	11.00	0.050
Measles 10d	UNICEF	1	40%	23.50	0.226
OPV 20d	UNICEF	3	20%	7.28	0.155
DTP-HepB-Hib 2d	UNICEF	3	10%	38.50	3.500

a. Wastage and cost data obtained via written correspondence with the Uganda EPI management staff (January 2010).
b. Tertiary vaccine packaging figures based on bulking factor of comparable WHO prequalified vaccines.

Abbreviations/acronyms: FIP= fully immunized person; BCG= Bacilles Calmette-Guérin; d=dose; UNICEF= United Nations Children's Fund; TT= tetanus toxoid; OPV= oral polio vaccine; DTP-HepB-Hib= diphtheria-tetanus-pertussis-hepatitis B-*Haemophilus influenzae* type b.

Based on written correspondence from PATH's Vietnam office (October 2009) and EPI management staff (January 2010), the syringe wastage rate is assumed to be 10%, and the safety box over-order rate is 150% for both countries.

Vaccine vial size assumptions

Storage and transport of temperature sensitive vaccines can be costly, especially if additional refrigeration equipment needs to be procured to meet cold chain capacity requirements. Thus, introduction of new vaccines in multidose versus single-dose presentations offers significant volume savings in the cold chain and reduces the volume of packaging waste. However, in order for this to translate to a true cost savings, the additional cost of vaccine wastage associated with multidose presentations needs to be offset by the savings related to cold chain volume. This becomes particularly difficult with vaccines in multidose containers that cannot be kept for more than one vaccine session after opening due to either the lack of preservative in the containers or to difficult immunization logistics.

The VPAT is able to take into account principle components related to the delivery of a vaccine from the national level all the way down to the health facility level. When the total cost per dose to deliver a vaccine presented in a multidose vial or compact prefilled syringe is equal to or lower than the total cost per dose to deliver vaccine from a single-dose vial, then the presentation is deemed to be economically viable. The VPAT determines this viability by calculating the break-even wastage rate for each presentation based on the average wastage rate for a single-dose vial in a particular country. To calculate the breakeven wastage rate, the cost per dose for each alternative presentation is set equal to the cost per dose of the single-dose vial. If the breakeven wastage rate for a given HPV vaccine presentation is considered achievable for the particular immunization strategy in the country, then that presentation is considered viable.

Since the interpretation of the breakeven wastage rate is driven by vaccine price per dose and target wastage rates, defining a reasonable price per dose and rational target wastage rate is critical. To account for the impact of price per dose, a sensitivity analysis using a range of potential developing country vaccine prices is used. To account for the impact of target wastage rates, two sets of wastage data were used—HPV vaccine wastage and proxy vaccine wastage—for each country. The first data set utilizes reported and calculated wastage rates from the HPV vaccine introduction studies in Vietnam and Uganda (Analysis 1) which are available for all presentations except the ten-dose vial with preservative. The second data set utilizes average reported proxy wastage rates from national immunization program vaccines of the same vial size in Vietnam and Uganda or comparable country studies (Analysis 2).

Analysis 1: Leveraging HPV vaccine introduction data

Analysis 1 leverages actual single-dose vial wastage rates and session sizes reported from school-based HPV vaccine introduction in Vietnam and Uganda (see Figures 1–2). Estimated wastage rates for Uniject and two-dose vials were calculated using the collected single-dose wastage rates and corresponding frequency and size of vaccination session (see Tables 4–5). These reported and estimated HPV vaccine wastage rates were

used as benchmarks in the VPAT break-even analyses. Wastage rates for ten-dose vials could not be extrapolated from the study data.

Figure 1. Frequency of Vietnam HPV vaccine administration sessions

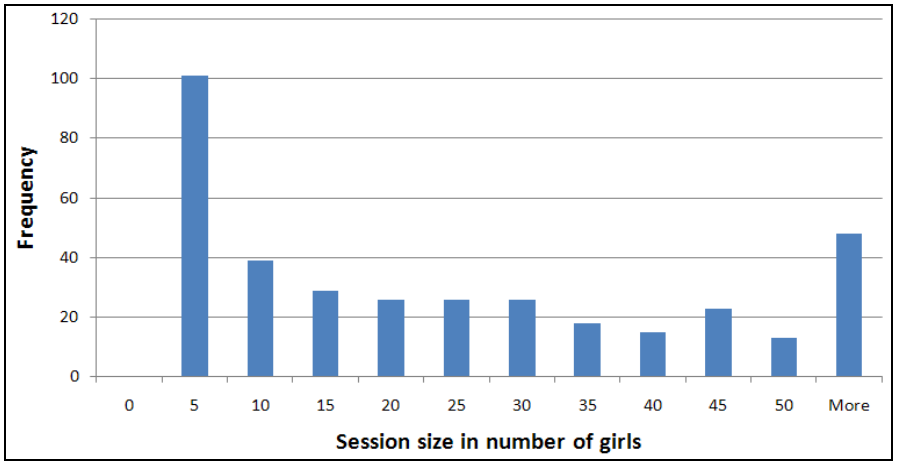


Table 4. Reported and estimated vaccine wastage for alternative vial sizes without preservative, PATH HPV vaccination demonstration projects, Vietnam, 2008 to 2009[7]

	Vial size	Doses wasted	Doses analyzed	Percent wastage
Reported wastage	Single-dose vial	101	10,273	1.0%
Calculated wastage	Uniject	101	10,273	1.0%
	Two-dose vial	175	9,143	1.9%

Figure 2. Frequency of Uganda HPV vaccine administration sessions

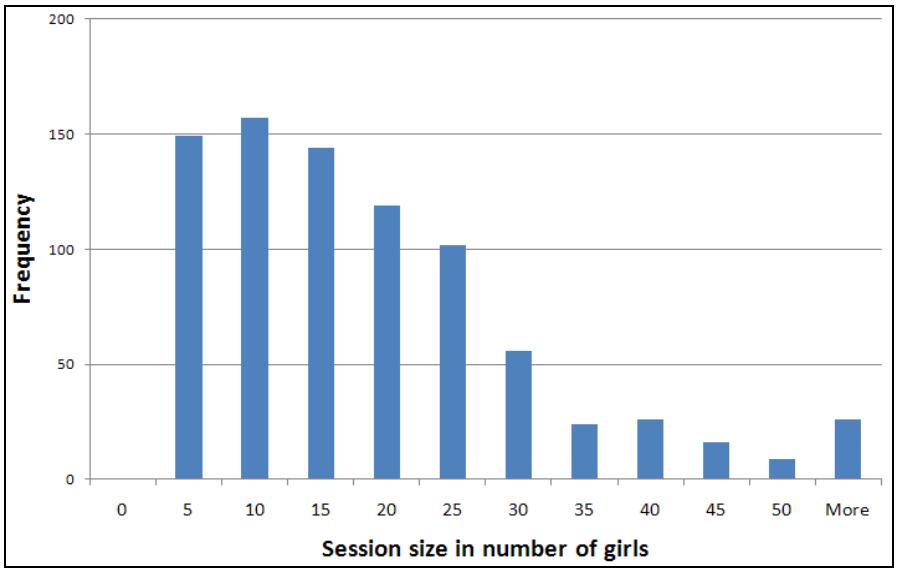


Table 5. Reported and estimated vaccine wastage for alternative vial sizes without preservative, PATH HPV vaccination demonstration projects, Uganda, 2008 to 2009[7]

	Vial size	Doses wasted	Doses analyzed	Percent wastage
Reported wastage	Single-dose vial	116	15,860	0.7%
Calculated wastage	Uniject	116	15.860	0.7%
	Two-dose vial	399	14,013	2.8%

The advantage of these wastage targets is that they are specific to Vietnam and Uganda and delivery of community- and school-based HPV vaccine immunization strategies. However, the reported wastage may represent a rate that is superior to typical country routine or campaign immunization strategies, given the vigilance and resources involved in introduction studies.

Analysis 2: Leveraging proxy wastage rates

Given the novelty of the new vaccine and rigor in which the introduction work was undertaken, a second model run was performed using more conservative wastage rate estimates. Analysis 2 leveraged reported vaccine wastage rates from comparable vaccine presentations used in Vietnam and Uganda or other comparable studies (see Tables 6–7). The benchmark for two-dose vials was based on Vietnam and Uganda reported wastage rates for hepatitis B (HepB) and pentavalent vaccine (two-dose vial liquid DTP-HepB with lyophilized *Haemophilus influenzae* type b), respectively. Given that Vietnam vaccinates children one day per month, it is assumed that this two-dose presentation is discarded following an immunization session. Thus, in Vietnam, a two-dose HepB vaccine with preservative will follow the same protocol as a two-dose vial of HPV vaccine without preservative. Similarly, since Uganda's pentavalent vaccine is lyophilized and requires disposal several hours after reconstitution, this analysis assumes two-dose pentavalent will follow the same protocol as a two-dose vial of HPV vaccine without preservative.

Since neither country currently uses vaccines in single-dose vials or compact prefilled syringes, reported wastage rates from published studies were utilized as a proxy. The target for single-dose vial wastage is based on the median wastage rates of seven single-dose vial liquid pentavalent vaccines from four low-income countries published in a recent study.[8] The benchmark for ten-dose vials is based on the median wastage rates of eight HepB and DTP vaccines in ten-dose vials with preservative across four low-income countries.[8] It is assumed that a theoretical ten-dose vial of HPV vaccine would contain preservative as well. Uniject target wastage rates for both analyses were based on reported wastage rates from a published study in Indonesia using HepB vaccine in Uniject.[9]

Table 6. Vietnam reported vaccine wastage rate proxies

Vial size	Percent wastage	Proxy source
Single-dose vial	5%	Median wastage of seven pentavalent vaccines[8]
Uniject	1%	HepB vaccine Indonesia[9]
Two-dose vial	5%	HepB vaccine Vietnam[a]
Ten-dose vial with preservative	10%	Median wastage of eight DTP, or HepB vaccines[8]

a. Data obtained are based upon written correspondence from PATH's Vietnam office (October 2009).

Abbreviations/acronyms: HepB= hepatitis B; DTP= diphtheria-tetanus-pertussis.

Table 7. Uganda reported vaccine wastage rate proxies

Vial size	Percent wastage	Proxy source
Single-dose vial	5%	Median wastage of seven pentavalent vaccines[8]
Uniject	1%	HepB vaccine Indonesia[9]
Two-dose vial	10%	DTP-HepB+Hib vaccine Uganda[a]
Ten-dose vial with preservative	10%	Median wastage eight DTP, HepB vaccines[8]

a. Data obtained are based upon written correspondence from the Uganda EPI management staff (January 2010).

Abbreviations/acronyms: HepB= hepatitis B; DTP-HepB+Hib= liquid diphtheria-tetanus-pertussis-hepatitis B+lyophilized *Haemophilus influenzae* type b.

Vaccine distribution and storage assumptions

The actual cost of future HPV vaccines for developing countries is not known at this time, so a range of prices was chosen to explore the price sensitivities relative to presentation. Prices per dose of $1.50, $3.50, $7.50, $10.00, and $15.00 were selected for the model. For the purpose of this analysis, the model assumes that shipping and freight charges are included in the price. No price differential between presentations is also assumed. Thus, presentations are priced the same on a per dose basis. In a real market setting, however, the price and price differential variables are defined by the manufacturer based on predicted market demand. For example, manufacturers of a higher cost delivery device may minimize the price differential in order to capture market share. For a high price vaccine, a manufacturer using this strategy should be able to achieve a sufficient profit margin despite potential higher variable costs of goods.

In order to calculate the total distribution cost per dose, assumptions related to the vaccine delivery schedule, standard cold chain equipment, and energy costs at each level of distribution were provided by PATH's Vietnam team and EPI Management staff in Uganda (see Tables 8–15).

Table 8. Vaccine delivery schedule for Vietnam[a]

Storage level	Vaccine arrival frequency (every x months)	Mode of transport	Mean travel distance (km)
National (n=1)	5.0	Airplane, car	1068
Regional (n=4)	3.5	Airplane, car	250
Provincial (n=63)	2.5	Car	50
District (n=671)	1.0	Car, motorbike	25
Commune (n=10,876)	1.0	Motorbike, bicycle	10

a. Data obtained are based upon written correspondence from PATH's Vietnam office (October 2009).

Table 9. Vaccine delivery schedule for Uganda[5,10]

Storage level	Vaccine arrival frequency (every x mo)	Mode of transport	Mean travel distance (km)
Central vaccine store (n=1)	3.0	4x4, trucks	11,094
District vaccine store (n=80)	1.0	Pickups	960
Health subdistrict (n=214)	1.0	Pickups, motorcycles	600
Health units (n>400)	1.0	Motorcycles, bicycles	144

Table 10. Standardized cold chain equipment for immunization in Vietnam[a]

Storage level	Cold chain equipment	Peak utilization
National	Cold room/freezer room	100%
Regional	Cold room/freezer room	100%
Provincial	Ice-lined refrigerator (Electrolux TCW-3000) and domestic refrigerators	65%
District	Ice-lined refrigerator (Electrolux TCW-3000) and domestic refrigerators	65%
Commune	Cold box, vaccine carrier	65%

a. Data obtained are based upon written correspondence from PATH's Vietnam office (October 2009).

Table 11. Standardized cold chain equipment for immunization in Uganda[a]

Storage level	Cold chain equipment	Peak utilization
Central Vaccine Store	Four cold rooms/one freezer room	100%
District Vaccine Store	Ice-lined refrigerator, Sibir GE, electric freezer, cold boxes	100%

Storage level	Cold chain equipment	Peak utilization
Health subdistrict	Ice-lined refrigerator, Sibir GE, electric freezer, cold boxes, solar refrigerator	80%
Health units	Vaccine carriers, Sibir GE, solar refrigerator	80%

a. Data obtained are based upon written correspondence from the Uganda EPI management staff (January 2010).

Based upon written correspondence from PATH's Vietnam office (October 2009) the economic life of cold rooms and freezer rooms is estimated to be 15 years and the economic life of refrigerators is estimated to be ten years for both countries.

Table 12. Vietnam energy costs[11]

Fuel type	US$ per unit
Electricity (kWh)[a]	0.040
Diesel oil (liter)	0.717
Gas (liter)	0.851
Kerosene (liter)	0.773

a. Electricity data in this table is based upon written correspondence from PATH's Vietnam office (October 2009).

Table 13. Uganda energy costs[a]

Fuel type	US$ per unit
Electricity (kWh)	0.2
Diesel oil (liter)	1.0
Gas (liter)	2.0
Kerosene (liter)	NA

a. Data obtained are based upon written correspondence from Uganda EPI management staff (January 2010).

Table 14. Vietnam distribution costs[a]

Storage level	Mode of transport	Cost ($/m³/km)	Avg cost ($/m³/km)
National	Airplane	1.730	1.315
	4x4	0.900	
Regional	Airplane	1.730	1.315
	4x4	0.900	
Provincial	Truck	0.820	0.820

Storage level	Mode of transport	Cost ($/m³/km)	Avg cost ($/m³/km)
District	Car	0.350	0.248
	Motorbike	0.145	
Commune	Motorbike	0.145	0.087
	Bicycle	0.028	

a. Data obtained are based upon written correspondence from PATH's Vietnam office (October 2009).

Table 15. Uganda distribution costs[12]

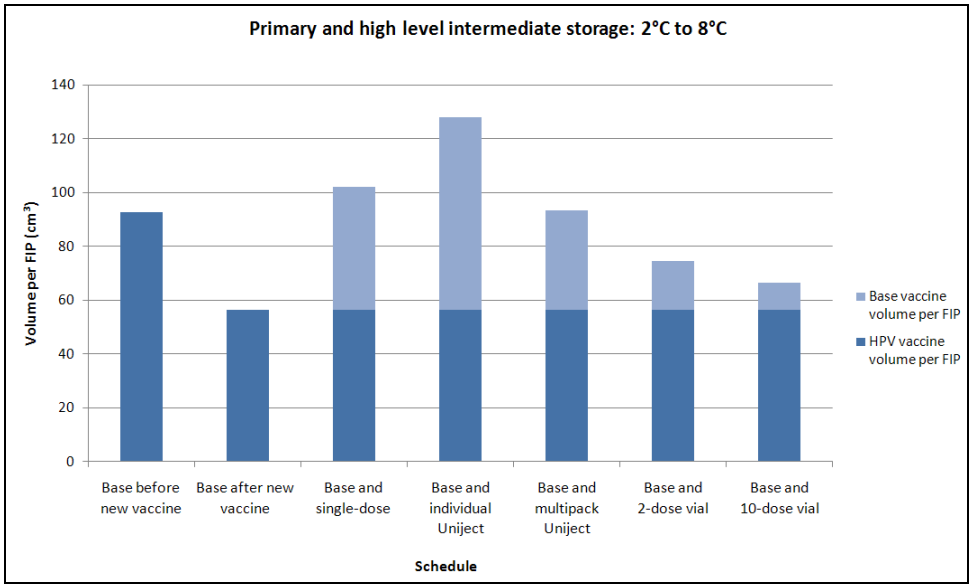
Storage level	Mode of transport	Cost ($/m³/km)	Avg cost ($/m³/km)
Central	4x4	0.142	0.085
	Trucks	0.029	
District	Pickups	0.127	0.127
Health subdistrict	Pickups	0.197	0.173
	Motorcycles	0.149	
Health units	Bicycles	0.028	0.028

Results

Volume analysis

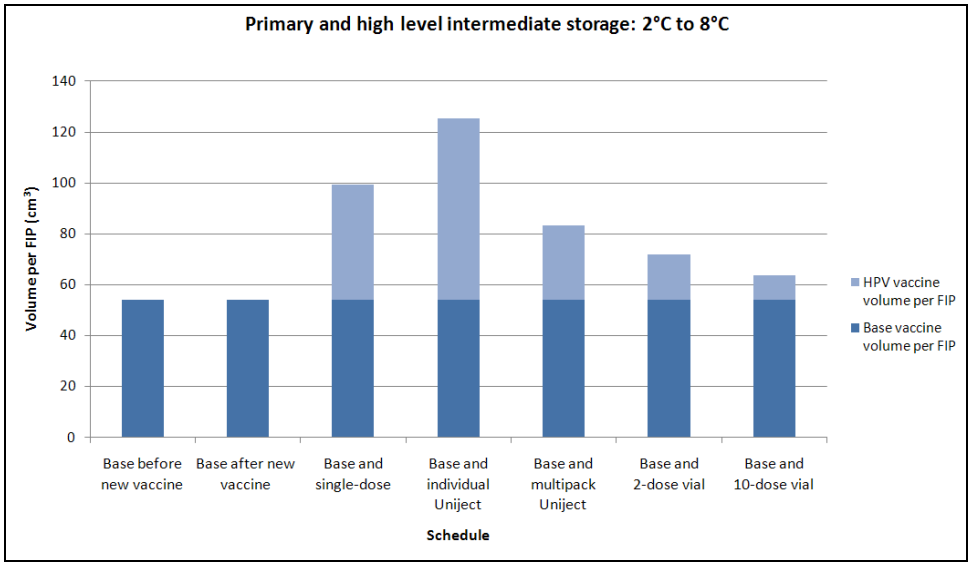
The VPAT analysis compares six scenarios per FIP: 1) base or current national immunization vaccine schedule, referred to as "base," 2) base and HPV in single-dose vials, 3) base and HPV in individually packed Uniject, 4) base and HPV in multipack Uniject, 5) base and HPV in two-dose vials, and, 6) base and HPV in ten-dose vials (with preservative). Given the reported and published routine vaccine wastage rate benchmarks in Vietnam, storage volume per FIP in the cold chain at the central and regional levels would increase most for individually packed Uniject (126%) and single-dose vials (80%). Volume per FIP in the cold chain would only increase slightly for multipack Uniject (65%), two-dose vial (32%), and ten-dose vial (17%) presentations (see Figure 3). At the health facility, or commune level, the trend is similar with individual-pack and multipack Uniject, single-, two-, and ten-dose vials increasing storage per FIP by 100%, 51%, 64%, 25%, and 14%, respectively. Shipping volumes follow a similar pattern, causing a volume increase for transport of 46% for individually packed Uniject, 23% for multipack Uniject, 29% for single-dose vials, 11% for two-dose vials, and 6% for ten-dose vials.

Figure 3. Cold chain storage volume at the central and regional levels in Vietnam



In Uganda, assuming routine vaccine wastage rates are maintained, the addition of HPV vaccine will increase storage volume per FIP at the central, district, and health subdistrict levels most significantly with individually packed Uniject (132%) and single-dose vials (84%). Volume per FIP in the cold chain would only increase slightly for multipack Uniject (68%), two-dose vial (33%), and ten-dose vial (18%) presentations (see Figure 4). At the health-unit level the trend is similar with individual-pack and multipack Uniject, single-, two-, and ten-dose vials increasing storage per FIP by 107%, 55%, 68%, 27%, and 15%, respectively. Shipping volumes follow a similar pattern, causing a volume increase for transport of 34% for individually packed Uniject, 18% for multipack Uniject, 22% for single-dose vials, 9% for two-dose vials, and 5% for ten-dose vials.

Figure 4. Cold chain storage volume at the central and health district levels in Uganda



Syringes and safety boxes occupy significant volume and therefore may greatly impact the overall supply chain cost. To understand the extent of this impact (and since Vietnam distributes syringes separately from vaccines), this analysis modeled the supply chain costs with syringes included in distribution and without (no distribution cost from national to provincial levels). Ultimately, distributing syringes and safety boxes with vaccines or separate from vaccines did not affect the results.

Vial size analysis

Analysis 1: Leveraging HPV vaccine introduction data

With only 1% wastage for single-dose vials reported from the Vietnam HPV vaccine introduction, the VPAT analysis demonstrates that individually packed Uniject is not an economically viable option compared to single-dose vials at any of the vaccine price points tested. In contrast, multidose Uniject and two-dose vials are feasible presentation options at all price points tested (see summary in Table 16).

Based on the HPV vaccine introduction data for Uganda which resulted in 0.7% wastage for single-dose vials, the VPAT analysis shows that individually packed Uniject is not an economically feasible option at any of the vaccine prices tested. However, multipack Uniject is economically feasible at all vaccine price points tested. A two-dose vial is a feasible presentation option if the price per dose of HPV vaccine is less than $7.95 (see summary in Table 16).

Should manufacturers succeed in creating an HPV vaccine that is thermostable at ambient temperatures, single-dose presentations would become slightly more attractive from a product and supply chain cost perspective, and multidose vials become slightly less attractive (see Table 16 and 17). This is the case in both Vietnam and Uganda: as the demand for costly cold storage space declines, the distribution costs of Uniject become less prohibitive and the space saving benefit of multidose vials is less influential from a cost comparison perspective.

Table 16. Vietnam and Uganda HPV vaccine introduction target wastage and VPAT breakeven price

	Vietnam			Uganda		
Vial size	**Demo trial wastage**	**VPAT breakeven price**		**Demo trial wastage**	**VPAT breakeven price**	
		5°C	**Ambient**		**5°C**	**Ambient**
Single-dose vial	1.0%			0.7%		
Individual Uniject	1.0%	>$15.00	>$15.00	0.7%	>$15.00	>$7.50
Multipack Uniject	1.0%	All prices tested	All prices tested	0.7%	All prices tested	All prices tested
Two-dose vial	1.9%	All prices tested	All prices tested	2.8%	<$7.95	<$6.25

Note: Prices tested included $1.50, $3.50, $7.50, $10.00, and $15.00 per dose.

Abbreviations/acronyms: VPAT= Vaccine Presentation Assessment Tool.

Analysis 2: Leveraging proxy wastage rates

For Vietnam, using an average of 5% wastage for single-dose vials and target proxy wastage rates, individually packed Uniject reaches parity with a single dose vial at price points greater than $2.60 per dose. Multipack Uniject, however, is economically viable at all price points tested. Assuming that two-dose vials have the same wastage rate as single dose vials, two-dose vials are economically viable at all price points tested. Given the target proxy wastage rate of ten-dose vials with preservative, the HPV vaccine multidose presentation is considered economically viable compared to single-dose vials at prices less than $2.10 per dose (see Table 17). Across the price points tested, the results in Vietnam are not affected with the addition of pentavalent and removal of HepB and DTP vaccines.

For Uganda, using a 5% average wastage rate for single-dose vials and target proxy wastage rates, individually packed Uniject breaks even with the single dose vial at any vaccine price point greater than $1.20 per dose. Uniject in multipacks, however, is a viable presentation option at all price points tested. Two-dose vials break even with single-dose vials at less than $3.20 per dose, and ten-dose vials with preservative are economically viable when compared to single-dose vials if priced at less than $0.39 per dose (see Table 17).

Table 17. Vietnam and Uganda reported wastage rate proxies and VPAT breakeven price

	Vietnam			Uganda		
Vial size	**Reported wastage**	**VPAT breakeven price**		**Reported wastage**	**VPAT breakeven price**	
		5°C	**Ambient**		**5°C**	**Ambient**
Single-dose vial	5%			5%		
Individual Uniject	1%	>$2.60	>$2.10	1%	>$1.20	All prices tested
Multipack Uniject	1%	All prices tested	All prices tested	1%	All prices tested	All prices tested
Two-dose vial	5%	All prices tested	All prices tested	10%	<$3.20	<$2.50
Ten-dose vial with preservative	10%	<$5.50	<$5.00	10%	<$3.95	<$3.00

Note: Prices tested included $1.50, $3.50, $7.50, $10.00, and $15.00 per dose.

Abbreviations/acronyms: VPAT= Vaccine Presentation Assessment Tool.

The VPAT results from Vietnam and Uganda begin to provide insight into key variables that should be considered when defining the attributes of future vaccines targeting low-resource settings. Both countries reveal sensitivities around country distribution costs ($/$m^3$/km), particularly at the first and second tiers of the supply chain. This is likely the result of high capital costs and operating costs associated with large transport vehicles. Estimated life and percent utilization of transport and cold chain equipment are also associated key outcome drivers. Volume of secondary packaging, if adjusted, could have

a dramatic impact on the cost viability of a presentation, as illustrated with the individual- versus multipack Uniject. Finally, more thermostable vaccines result in low-dose presentations becoming more economically viable and ten-dose presentations becoming less economically viable.

General applicability across developing countries

Access to data inputs from several developing countries of geographically representative large populations may be leveraged to draw general recommendations on vaccine presentation and packaging for resource constrained countries. Should the model be adapted to incorporate information from multiple countries and predict the most cost-efficient size and characteristics for the majority of developing countries, several additional modifications may be considered. For instance, the impact of session size, application of WHO multidose vial policy (MDVP), and immunization strategy are taken into account when interpreting the feasibility of a breakeven wastage rate, but instead may be incorporated into the model calculations. In addition, the model should be capable of accounting for more than one type of cold chain equipment or form of transport at each level of the supply chain. Inclusion of capital costs, insurance, maintenance, and operating costs inherent in distribution costs may improve transparency. Finally, the model assumes all vaccines are transported at the same frequency and through the same supply chain sequence—flexibility of schedule and routes for different vaccines would be ideal.

Summary and conclusions

Based on the available data from the HPV introduction studies in Vietnam, multipack Uniject, single-, or two-dose vials may be the preferred option over ten-dose vials for HPV vaccine delivery at most vaccine price points. In Uganda, multipack Uniject or single-dose vials prove to be economically viable at all price points tested. The viability of two-dose vials depends on the price of HPV vaccine remaining less than $7.95 per dose. Ten-dose vials with preservative and adoption of the MDVP are economically viable when HPV vaccine is priced at $5.50 per dose or less in Vietnam and $3.95 per dose or less in Uganda.

Given the low wastage rates achieved in the HPV vaccine introductions, the vaccine would need to be priced higher than $15.00 per dose for it to be packaged in individually packaged Uniject and have a distribution cost comparable to that of single-dose vials. The space and cost saved by not needing a separate autodisable syringe does not sufficiently compensate for the larger packaging associated with Uniject packed individually in a foil pouch. However, revised packaging of Uniject using multipacks has led to per dose vaccine packaging volumes smaller than that of single-dose vials. According to the VPAT, manufacturers distributing HPV vaccine in the new, smaller size Uniject to Vietnam and Uganda may consider adding a $0.21 and $0.18 per dose price premium, respectively, over single-dose vials. This suggested price differential, however, needs to be substantiated with a thorough demand and pricing analyses.

Finally, should air transport become more cost-effective in Vietnam or should four-wheel drive vehicles become better utilized in Uganda, larger versions of compact prefilled devices may be considered economically viable options.

Until further investment in data collection and analysis is undertaken, the assumptions used in this analysis are country specific. It should also be noted that this report represents one of many variables involved in choosing the most appropriate vaccine presentation; ease of use, safety, ergonomics, and many other factors may influence country decision-makers.

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