

Policy Development for Human Papillomavirus Vaccine Introduction in Low-Resource Settings

Jennifer Tsui¹, D. Scott LaMontagne², Carol Levin², Allison Bingham^{2,*} and Lysander Menezes³

¹University of California at Los Angeles, School of Public Health, Department of Health Services, Box 951772, Los Angeles, CA 90095-1772, USA

^{#2}PATH, 1455 NW Leary Way, Seattle, WA 98107-5136, USA

^{#3}PATH, A-9, Qutab Institutional Area, U.S.O. Road, New Delhi 110 067, India

Abstract: The objectives of this analysis are: (1) to describe the policy environment related to human papillomavirus (HPV) vaccine introduction; (2) to identify the policy processes and key stakeholders in HPV vaccine introduction; (3) to summarize specific characteristics about HPV vaccines and their introduction that may be barriers to introduction; and (4) to recommend advocacy strategies to achieve a positive environment for cervical cancer prevention.

This descriptive qualitative study of HPV vaccine policy development used an iterative, inductive, theme-based approach to data analysis. The study was conducted in four developing countries—India, Peru, Uganda, and Vietnam. Study participants were comprised of a total of 237 national policymakers, legislators, officials, and senior managers from ministries of health, finance, and planning; leaders of medical and health professional associations; cancer institutes; heads of nongovernmental organizations; and women's health advocates.

While differences existed among low-income countries in specific cervical cancer, women's health, adolescent health, or immunization policy environments, we found the policymaking process itself, specific concerns related to HPV vaccines, and the information needs of policymakers for HPV vaccine introduction to be strikingly similar. Data on burden of cervical cancer, HPV vaccine safety and efficacy, and cost-effectiveness and vaccine affordability were top issues reported by policymakers. Advocacy strategies need to address these issues in order for HPV vaccine policy formulation and approval to be successful.

INTRODUCTION

Cervical cancer is the second most common cancer in women in the world, with nearly half a million new cases each year and more than 270,000 deaths annually [1], the majority of which occur in developing countries [2]. About 70 percent of cervical cancer cases are caused by human papillomavirus (HPV) types 16 and 18 [3]. While developed countries have experienced declines in cervical cancer mortality due to widespread Papanicolaou testing, developing countries face considerable logistical and financial barriers to establishing routine screening programs [4]. Highly efficacious vaccines for HPV 16 and 18 provide an opportunity for primary prevention of cervical cancer [5-7].

Researchers have noted that developing countries traditionally experience delays in new vaccine adoption [8-11].

Common reasons cited are financial constraints and political obstacles interfering with market forces [8], competing health priorities [10], absence of national disease burden data illustrating the magnitude of the problem [8], lack of country-specific vaccine efficacy data for their population [8, 11], and concerns about sustainable supply for new vaccines [9].

As new vaccines become available, the development and enactment of new vaccine policy regarding adoption, use, delivery, and financing are essential [12]. Development of new vaccine policy requires ongoing translation of information between scientific communities and policymakers, comprehensive assessment of new vaccine introduction capacity, and multiple iterations of policy formulation [8, 13, 14]. Addressing policymakers' needs for vaccine technical information, evaluations of cost and cost-effectiveness, and assessment of national capacity for introduction are key ingredients to success [15, 16]. Unfortunately, few studies present empirical data detailing this policy development

*Address correspondence to this author at PATH, 1455 NW Leary Way, Seattle, WA 98107-5136, USA; Tel: +1-206-285-3500; Fax: +1-206-285-6619; E-mail: abingham@path.org

[#]“Program for Appropriate Technology in Health”

process in low-resource settings. One example of a study that does achieve this level of analysis is Munira and Fritzen's policy process report on early hepatitis B vaccine adoption in Thailand and Taiwan [12]. In their assessment, a broad range of information related to vaccine characteristics, health systems, and policy actors must be considered in a country-specific context for vaccine adoption at the national level [12]. Another example comes from DeRoeck's report on the Disease of the Most Impoverished (DOMI) Program and dengue fever [17]. DeRoeck uses data from surveys of policymakers to assess how new vaccines fit into the priorities of disease-control programs in low-resource settings [17].

This paper analyzes policy data gathered through formative research conducted in India, Peru, Uganda, and Vietnam as a part of the five-year *HPV Vaccines: Evidence for Impact* project led by PATH. This project studied the sociocultural milieu, health system structures, and policy environments related to cervical cancer and HPV. Our analysis reviews the individual policy environment assessments and focuses on similarities and differences between the countries to meet four objectives: (1) to describe the policy environment related to HPV vaccine introduction, (2) to identify the policy processes and key stakeholders in HPV vaccine introduction, (3) to summarize specific characteristics about HPV vaccines and their introduction that may be barriers to introduction, and (4) to recommend advocacy strategies to achieve a positive environment for cervical cancer prevention.

METHODS

This descriptive qualitative study analyzed formative research on HPV vaccine policy in four countries. The purpose of the formative research was to inform HPV vaccine pre-introduction planning, including country-level HPV vaccine delivery strategies, communication messages, and advocacy plans. The full methodology and rationale for the larger body of formative research is published elsewhere; [18] however, below we provide a brief discussion of the conceptual model that informed the formative research as well as highlights of the methods employed for the policy component.

The Ecological Conceptual Framework

The formative research on HPV vaccine policy was grounded in an "ecological conceptual framework," which recognizes that individual health behaviors occur within an interplay of five levels of influence: (1) the individual, (2) interpersonal family dynamics, (3) community norms, (4) institutional structures, and (5) the policy environment [19, 20]. An ecological conceptual framework is often used in health services research because it is a useful means of depicting the different levels of individual and social factors involved in health care planning, delivery, and decision-making. While other conceptual frameworks are used in health services research as well, the ecological model provided the most valuable framework for the larger study on HPV vaccine policy in low-resource settings. It was an

effective tool to guide the aims of the study; to allow for cross-country comparisons; and to identify information needs and generate evidence for decision-making and operational planning [18]. More specifically for this paper, the ecological approach enabled us to clearly understand the various types of influencing forces that could determine a country's movement towards policy formulation for introduction of the HPV vaccine.

Study Populations

The study populations at the policy level included national policymakers, legislators, ministry of health (MOH) officials (including heads of epidemiology, gynecology, maternal and child health, cancer control, and immunization), key officials in finance and planning ministries, leaders of medical and health professional associations, cancer institutes, heads of nongovernmental organizations (NGOs), and women's health advocates (Table 1). Local research teams in each country developed specific criteria to select participants who were appropriate in the local context of HPV vaccine policymaking [21, 22]. These criteria were especially important at the policy level of the formative research, as key positions and organizations involved with vaccine policy varied from country to country. Key informants were selected for in-depth interviews using this criteria-based approach, which selected for knowledge of the decision-making process related to cervical cancer prevention or vaccine introduction, or ability to influence this process. In India, for example, stakeholders in the health policy space were broadly classified into policymakers and policy influencers. Policymakers were defined as technical experts and generalists within government who would develop the discursive formation on issues and participate in formulating policy. Policy influencers were defined as technical, communication, and advocacy specialists. Participants from Peru, Uganda, and Vietnam also encompassed this spectrum of policymakers and policy influencers.

Data Collection and Sources

This analysis used data from unpublished formative research technical reports produced by research teams in each of the four project countries [23-28]. The formative research was conducted from 2006 to 2008. Data collection included desk reviews and in-depth interviews. Desk reviews consisted of careful assessment of existing government policy and technical documents related to national health statistics, school attendance reports, national policy guidelines for cervical cancer and/or new vaccine introduction, multiyear plans for immunizations, performance reports, vaccine delivery information, vaccine financing data, women's health, reproductive health, adolescent health and school health policies, and other documents of relevance. In-depth interviews explored understanding, perspectives, and experiences related to child health and well-being, vaccines, and cervical cancer, as well as the policy environment affecting these issues.

Table 1. Sample Population of Policymakers and Policy Facilitators

India	Peru	Uganda	Vietnam
Study Location			
Andhra Pradesh state: Khammam district	Ayacucho region	Gulu district	Dong Thap province
Gujarat state: Vadodara district	Piura region	Kampala district	Nghe An province
	Ucayali region	Masaka district	Thai Binh province
	Lima (large metropolitan area)	Mbarara district	Hanoi (large metropolitan area)
		Soroti district	Ho Chi Minh City (large metropolitan area)
Study Populations			
Local, state, and national policymakers and policy and project implementers	Local, regional, and national government representatives	District and national policymakers	Health and education personnel at the provincial level
Number of In-Depth Interviews			
67	25	77	68

Analysis of Data

The primary sources of data for this analysis were the complete technical reports prepared by the formative research teams in each of the four countries. These documents were analyzed as textual data. An inductive approach was used to identify key commonalities and differences related to HPV vaccine policy across countries; major analytic themes were established prior to any analysis of the data. These four analytic themes were developed based on policy themes noted in vaccine literature [8-10, 17, 29-32]: (1) the current policy environment surrounding cervical cancer, immunization, and health services for young adolescents; (2) the vaccine policy process related to decision-makers, external stakeholders, formulation and implementation, and financing strategies; (3) specific concerns of policymakers about HPV vaccines; and (4) the information needs for HPV vaccine introduction. These themes were based on major constructs present in the theoretical frameworks used for this policy analysis as well as major themes present in prior studies related to vaccine introduction in low-resource settings [33-38]. In order to further refine each of the major themes, subthemes were developed deductively, or after multiple iterative reviews of the formative research reports and existing themes (Table 2). Themes and subthemes were identified and reviewed by all authors multiple times. Results are presented according to these themes and subthemes.

RESULTS

Policymakers and policy facilitators were interviewed in the following distribution: 67 from India, 25 from Peru, 77 from Uganda, and 68 from Vietnam (Table 1). Respondents represented both national and subnational levels of the policymaking process.

Policy Environment

Cervical Cancer Burden

Policymakers in all four countries were generally aware of cervical cancer. Officials from Uganda and Vietnam mentioned the economic burden of cervical cancer on individuals and communities. Understanding of the link between HPV and cervical cancer was limited. The degree of actual knowledge about cervical cancer and the perception of availability of disease burden data were high among officials in Uganda and Vietnam, but limited among officials in Peru. In Uganda, cervical cancer burden data are available through a limited registry covering the greater Kampala area, which has been operational for more than three decades; however, the registry is not representative of the country. In Vietnam, cancer burden data are available from main cancer hospital registries in the north (Hanoi) and south (Ho Chi Minh City) areas of the country; as with Uganda, national representativeness is lacking. Other data sources report regional cancer registries in Lima and Trujillo, Peru [39]. In India, cervical cancer burden data are available from population-based and hospital-based cancer registries [40-42]. Reports for India, Uganda, and Vietnam indicated specific, enacted, or drafted policies that prioritize cervical cancer in relation to women's health or reproductive health; data collection from our study in Peru was limited on this point.

Cervical Cancer Control

Prior studies have identified barriers to national cervical cancer screening programs in developing countries to include reasons such as competing health needs, limited human and financial resources, underdeveloped health care services, gender disparities in health care access and health information, wars, poverty, and the nature of cytology-based screening tests [43]. Even though no country reported a

Table 2. Key Areas of Inquiry for Vaccine Policy Process Analysis

Theme	Subthemes and Content
Policy Environment	
Cervical Cancer Burden	Knowledge, attitudes, and practices regarding cervical cancer and HPV, social/economic impact, public awareness.
Cervical Cancer Control	Existing policies, priority within the health system, government's focus on issue, current state of prevention and control, existing infrastructure.
Adolescent Health Services	Knowledge, attitudes, and practices regarding young adolescent health, existing policies, priority within the health system, government's focus on issue, existing infrastructure.
Immunization Programs	Existing policies, priority within the health system, government's focus on issue, experiences with previous vaccination programs, existing infrastructure.
Policy Process	
Policy Development and Internal Actors	Internal decision-makers who propose, review, and enact vaccine policy. Essential collaborating government agencies and representatives. Primary processes, departments, and stakeholders involved in vaccine adoption, financing, implementation, and monitoring.
External Influencers	Stakeholders external to the policy process who can relay information and influence decision-making of internal stakeholders.
Vaccine Financing	Processes for identifying financing mechanisms. Interaction between external and internal actors to mobilize financial commitment for vaccine introduction.
Policy Implementation	National and local bodies involved in implementation, delivery, and monitoring of vaccine.
HPV Vaccine-Specific Issues	
Vaccine Characteristics	Efficacy, safety, duration, adoption by other countries, WHO prequalification and recommendation.
Economic Evaluation	Vaccine cost, affordability, financing mechanisms, procurement, sustainability, cost benefit, cost-effectiveness.
Implementation and Monitoring	Feasibility, availability of demonstration or pilot data, resources needed from existing infrastructure, health care capacity, training of health care professionals.
Social Concerns	Target population, acceptability, equity, demand, effect on other vaccine programs.
Special Considerations for HPV Vaccine Introduction	
Information Needs of Policymakers	Additional information related to scientific, economic, implementation, and social concerns.
Messaging	Strategies for accurate messaging to communities.
Advocacy to Policymakers	Information needs of policymakers, effective strategies to generate and maintain support for vaccine policy, crucial collaborations for introduction and financial commitments.
Partnerships	Perceptions about partnership needs with international organizations, multilateral organizations, and private sector for scientific, structural, or financial support.

national cervical cancer screening program, respondents recognized the importance of cervical cancer prevention, indicated by its inclusion in policies on women's health, reproductive health, or noncommunicable diseases. For example, Uganda is intending to include comprehensive cervical cancer prevention in its noncommunicable diseases policy, and policymakers from India cited the growing visibility of cervical cancer as an opportunity to build screening and prevention programs. While India and Peru have mostly opportunistic cervical cancer screening programs,

Vietnam has coordinated screening programs only in specific provinces or cities where local political leaders and advocates have instituted them.

Adolescent Health Services

Specific policies to improve adolescent health were not mentioned by respondents, although various adolescent health services were discussed. While India has official programs targeting adolescent health, such as the "womb to adolescence" program, officials in Peru indicated a clear lack

of priority for adolescent health. Many respondents indicated there were more pressing health priorities for young adolescent girls than preventing future cervical cancer, such as malnutrition (Peru) and anemia (India).

Immunization Programs

The infrastructure and policies related to immunization programs are largely built upon guidelines set by the Expanded Program on Immunization, a program initiated by the World Health Organization (WHO) that is focused on increasing the immunization rates of young children. Respondents universally agreed that vaccinations are an important and effective strategy for disease prevention. All countries had specific plans and strategies outlined in their national immunization policies. For example, in Peru, the National Sanitary Immunization Strategy outlines the political, technical, and administrative priorities of achieving immunization goals. The existence of widespread national immunization programs and reported successes in implementation demonstrated their perceived level of importance. National immunization advisory committees assisted in program planning and implementation. In relation to HPV vaccines, countries mentioned programs or policies in which HPV vaccination could be included, such as tetanus toxoid vaccination campaigns in Uganda. However, enthusiasm was tempered by challenges facing current immunization programs, such as competing priorities for new vaccine introduction (India, Vietnam), acquisition of sufficient and sustainable funding (Peru, Uganda, Vietnam), and public opposition to or mistrust of new vaccines (all countries).

Policy Process

Policy Development and Internal Actors

Consistently across all four countries, national vaccine policy development occurred in four stages: stage 1, advocacy and agenda-setting; stage 2, review of scientific evidence; stage 3, policy formulation and review; and stage 4, vaccine policy approval (Fig. 1). In stage 1, raising awareness often involves the exchange of information between policymakers and national medical and scientific communities as well as communication with the WHO. In India, for example, academic bodies such as the Indian Academy of Pediatrics and the Federation of Obstetrics and Gynecology Societies of India play important roles in relaying HPV vaccine information to policymakers. In addition, due to the experience of hepatitis B and Japanese encephalitis in parts of India, immunization experts stated that it would be important to build community trust by explaining the purpose of introducing a new vaccine and the role of key players, including manufacturers, funders, government organizations, and other stakeholders. For all countries, vaccine licensure by national drug regulatory authorities was also viewed as a mechanism to trigger awareness.

Once a new vaccine is on the policy agenda, technical advisory committees within the MOH review and evaluate the scientific evidence (stage 2). As an example, in Peru, the National Immunization Program has technical and consultative committees that work on national plans, technical documents, and proposals related to the national immuniza-

tion program. All countries indicated the data required at this stage include national disease burden, vaccine efficacy and safety, programmatic feasibility, monitoring abilities, delivery strategies, and vaccine cost and cost-effectiveness.

In stage 3, policy formulation and review, the MOH and the designated technical review body engage other ministries in drafting vaccine policy. Affordability of the vaccine and financing strategies are assessed by the ministry of finance, planning, or development in conjunction with review of the scientific and technical information. At this stage, countries often look to the WHO or recommendations in other countries to guide their own policy. All of our respondent countries revealed some confusion related to the WHO processes involved in new vaccine recommendations. As one policymaker from India stated, "Introducing the HPV vaccine in immunization policy would need support at the national level from policymakers, NTAGI [National Technical Advisory Group on Immunizations], and WHO prequalification...."—a misunderstanding of the difference between WHO manufacturer prequalification and WHO recommendations for vaccine use. During the WHO prequalification process, the quality, safety, and efficacy of a new drug are assessed based on product information provided by manufacturers to see if the drug meets quality drug standards established by WHO [44]. While WHO prequalification determines whether a drug meets quality standards, it does not provide any recommendations for use. The WHO recommendations for new vaccines are provided by a separate body of experts, the Strategic Advisory Group of Experts on Immunization, to develop formal WHO recommendations for vaccine use. In relation to policy formation, respondents from India and Uganda strongly preferred to incorporate HPV vaccines into and strengthen current health programs when introducing the vaccines rather than create a new program or policy.

Vaccine policy approval was the final stage in the policy development process. We found differences in the approval process between countries—in the case of India, between states—depending on whether the vaccine policy was completely new or an addition to an existing policy. For completely new policies, most countries indicated a need for parliamentary or legislative approval. For including HPV vaccine in an existing policy, usually only approval from the MOH was required.

External Influencers

During the first three stages of the vaccine policy process, an ongoing and important relationship exists with external influencers, such as WHO, the United Nations Children's Fund (UNICEF), the GAVI Alliance, international NGOs, and academic or scientific organizations. They may provide technical assistance, scientific review of research, international guidelines, financing, or advocacy to promote vaccine introduction. For example, policymakers in Vietnam emphasized the supporting role of international organizations in mobilizing the involvement of donors for vaccine financing. In addition, ongoing relationships with WHO or international NGOs may provide technical expertise to develop country-level vaccine recommendations or implementation strategies.

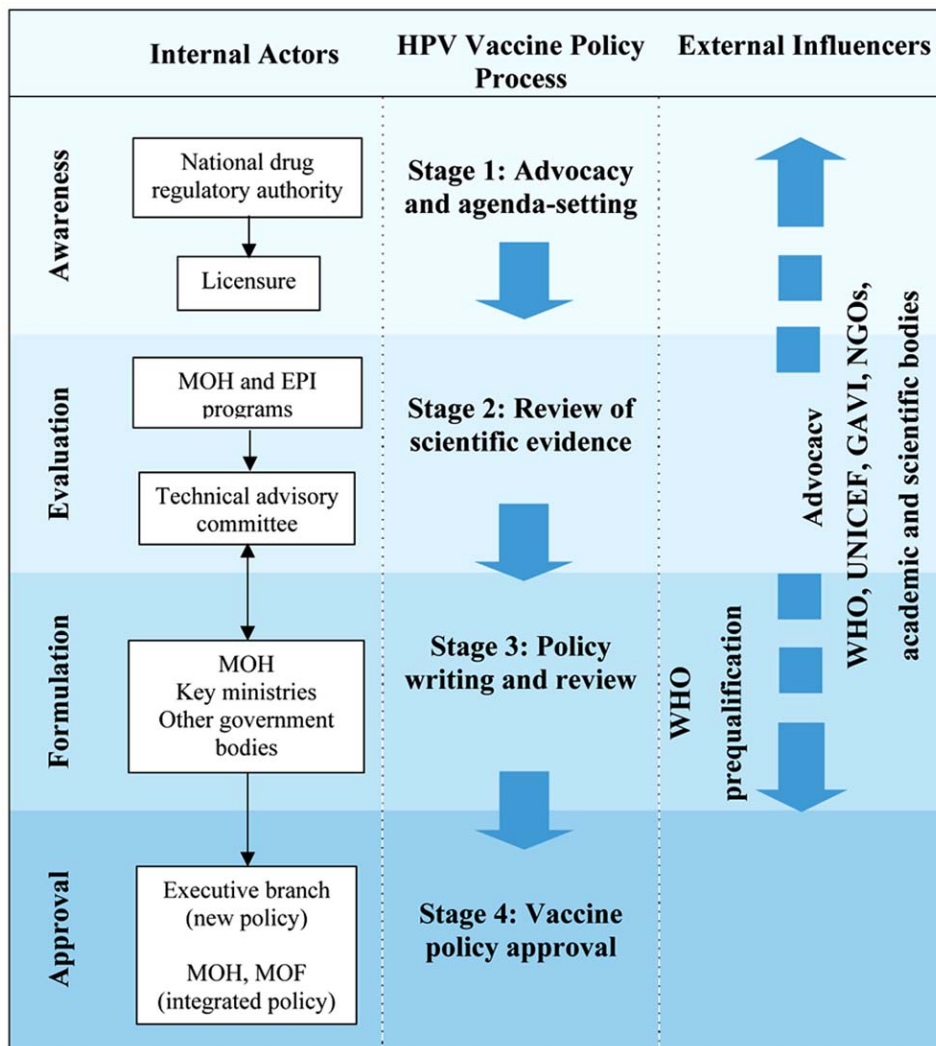


Fig. (1). Illustration of HPV Vaccine Policy Processes in India, Peru, Uganda, and Vietnam.

Note: EPI: Expanded Programme on Immunization (WHO, Geneva, Switzerland); MOF: Ministry of Finance; MOH: Ministry of Health.

Vaccine Financing

All countries had a national financing program for health priorities using both national and local funding. In the policy approval stage, the MOH estimates the budget required for introducing a new vaccine. For example, in Vietnam, the MOH consults the appropriate ministry (finance, economic planning, or development) to estimate new vaccine introduction costs and develop a budget for approval by higher authorities. A policymaker in Uganda stated, “The sources of funding are critical and should be very clear in the policy...additional resources would be required...to implement this new policy.” In India, the introduction of a new HPV vaccine occurs within the National Rural Health Mission, a major Government of India initiative that partners with the private sector to support vaccine financing. Approval of a budget is necessary to secure financial support from either domestic resources or international donors, such as the GAVI Alliance.

Policy Implementation

Even though all countries indicated that vaccine policy decision-making takes place mostly at the national level, countries differed on whether policy implementation was

directed nationally or locally. While India and Vietnam utilize iterative feedback between national and subnational levels during the policymaking and implementation processes, Peru and Uganda have more centralized implementation systems. Ad hoc technical committees are often formed to plan for the implementation of new vaccines. Regardless of whether a country decides to utilize an implementation advisory committee, all countries mentioned the need for collaboration between reproductive health, immunization, and school health programs.

HPV Vaccine-Specific Issues

Vaccine Characteristics

Policymakers in all countries expressed concern over the safety and efficacy of the vaccines. In particular, officials in India suggested the need for data from within the country as well as analysis of studies from other countries with similar disease profiles. Immunization experts from India emphasized the need for information on HPV vaccine price and efficacy, as well as the interaction of HPV vaccine implementation with other health programs to inform policymakers during the process. Respondents from Vietnam

were especially concerned about the lack of definitive data on the duration of vaccine effectiveness. Respondents from Uganda and Vietnam emphasized not wanting girls in their countries to be “guinea pigs” for HPV vaccine testing.

Economic Evaluation

Policymakers noted that evaluating the cost-effectiveness of HPV vaccines to prevent cervical cancer and modeling pricing schemes and affordability were necessary. Participants from India, Uganda, and Vietnam indicated cost and sustainability may be major barriers for HPV vaccine introduction in their countries because current prices appear unaffordable. Officials from Uganda also indicated concern regarding procurement and needed assistance from WHO and UNICEF.

Implementation and Monitoring

Implementation of HPV vaccines in school-based programs and clinic settings and the monitoring of vaccine uptake, feasibility of administration, and acceptability among eligible recipients were cited as important factors to consider by policymakers. Schools were mentioned by all respondents as a viable delivery mechanism for HPV vaccines. However, officials in India and Uganda mentioned potentially negative consequences with school introduction, such as jeopardizing other vaccination programs by competing for scarce resources like health worker time. Policymakers in India felt combining HPV vaccine delivery with schools may cause a problem, due to risk of incomplete or inappropriate management of adverse events, should they occur, as the school system was considered to not be adequately linked to the health system. Other delivery options mentioned included teen health programs (India), cervical cancer programs (India), and reproductive health services (Uganda). Respondents from Uganda and Vietnam were concerned about the mismatch of target age groups for HPV vaccines (10 to 12 years of age) and the current Expanded Programme on Immunizations populations (children younger than 5 years of age). Participants in Uganda and Vietnam suggested pilot projects to demonstrate there are no significant side effects and for better acceptability among individuals and policymakers.

Social Concerns

Policymakers were very specific in mentioning concerns related to how communities would perceive HPV vaccines. These social concerns included the age of the vaccine recipients, vaccine acceptability among parents and young adolescents, and overall perceptions regarding immunizations. Officials in Peru reported that some communities think the vaccine “might not be appropriate, as it could be too strong for the girls at their particular stage of development.” As a result, officials from Peru suggested disseminating data to the public on sexual initiation age and sexually transmitted infection. Some concern was raised regarding the possibility that the vaccine could encourage sexual activity. A member of parliament from Uganda said, “My other worry is the risk of implying that children can now engage in risky sexual behavior.” However, policymakers in all countries put much more emphasis on the possible adverse effects of the vaccine on fertility. For example, officials in Vietnam indicated that the long-term side effects of the vaccine and “how this

vaccine can impact girls’ fertility capacity in the future” are major concerns.

Special Considerations for HPV Vaccine Introduction

Information Needs of Policymakers

Policymakers from all countries mentioned the need for information related to disease burden, benefits of HPV vaccines, vaccine safety, side effects and efficacy, acceptability, cost, and financing specific to their countries. Of particular concern to policymakers from India was additional information on vaccine supply and safety, because these were seen as potential obstacles to successful introduction.

Messaging

We found remarkable consistency across all respondents regarding the necessity of an effective communication strategy to relay information on cervical cancer, and the nature, safety, and price of the vaccine, to all levels of society, including health care workers, communities, and individuals. All countries suggested mass media involvement, including radio and television, to deliver appropriate messages to communities. Accurate and convincing messaging is crucial for public acceptability of HPV vaccines—a point stressed by all respondents.

Advocacy to Policymakers

Respondents from India, Uganda, and Vietnam mentioned the need for high-level advocacy in support of vaccine introduction. Groups that could support this effort included academic bodies, medical associations, heads of state, first ladies, and other representatives in government. Participants in India and Peru mentioned grassroots organizations as partners in delivering advocacy messages. As one respondent from India noted, “[Cervical cancer deaths are] not eye-catching, visible, acute, or seasonal like deaths due to a vaccine-preventable disease like Japanese encephalitis.” Therefore, visualization of the impact of the disease on individuals and communities was recommended as an advocacy strategy. Respondents from Uganda and Vietnam indicated national- and district-level workshops led by the MOH and involving key stakeholders would be the most effective (and popular) way to translate information, advocate for HPV vaccine adoption, and mobilize support for policy development.

Partnerships

Partnerships were emphasized by all countries as being critical to success. Partnerships among government agencies included ministries of health, education, gender, and finance. Respondents from India and Uganda suggested public-private partnerships (with the commercial sector in the case of India and with private health care providers in Uganda) for assistance with resources and to reduce costs. Partnerships with external influencers, including WHO, UNICEF, GAVI, and the Pan American Health Organization were also cited as beneficial to vaccine policy development, implementation, and financing.

DISCUSSION

Understanding the current policy environment related to cervical cancer, reproductive health, adolescent health

services, and immunizations in developing countries is essential for identifying the decision-making process for HPV vaccine introduction and for gauging vaccine acceptability among policymakers. These contextual factors reveal potential receptivity of the current infrastructure, social institutional factors, environmental pressures, and inter-organizational networks germane to introducing new vaccines [36, 37].

Although multiple studies describing developing-country immunization programs exist, few detail the exact process for new vaccine policy development, especially for HPV vaccines. In fact, there are relatively few studies of health policy development processes of any kind in low-income countries [45]. The results of our study suggest that while differences exist among developing countries related to specific cervical cancer, women's health, adolescent health, or immunization policy environments, the policymaking process itself, specific concerns related to this vaccine, and information needs of policymakers for HPV vaccine introduction were strikingly similar. Policymakers from all countries voiced concerns regarding the potential fertility impact of HPV vaccines and misunderstanding of the vaccine as a disguise for contraceptive methods. These concerns were not only consistent across countries but also consistent with the results from sociocultural studies in these same countries, among girls, parents, health workers, teachers, and communities [46]. Even though countries were at different stages with cervical cancer programs, solid and positive experience with immunization could be leveraged as an opportunity to build support for prevention through vaccination.

Competing priorities for different health initiatives was an underlying theme in all countries for introduction of HPV vaccines. The information needs for policymakers focused on both the magnitude of the problem and the effectiveness of the solution; comparing problems and solutions for a variety of competing health priorities in the first stage of the policymaking process—awareness—may be an effective strategy for advocacy. As Shiffman *et al.* note, coalition-building can shape the dialogue with policymakers to position the disease and intervention of interest—in this case, HPV vaccines for the prevention of cervical cancer—in the context of these other priorities [47].

Countries rely on an interaction between internal policymakers and external influencers in the first three stages of the policy process for new vaccine introduction. Particularly important is the external influence of WHO, despite the widespread confusion between the prequalification process and WHO recommendations for vaccine adoption. The Strategic Advisory Group of Experts on Immunization has recently announced their support for public sector introduction of HPV vaccines and has requested that WHO produce a position paper for this recommendation [48].

While it was hypothesized that countries may emphasize differing concerns regarding HPV vaccines and special considerations relative to their policy development process and environment, results from our analysis indicate that most countries referenced the same top-priority issues: (1) data on the burden of cervical cancer, (2) HPV vaccine safety and efficacy, and (3) cost-effectiveness and vaccine affordability.

These findings are consistent with previous research that suggests the importance of empirical evidence in the policy-making process for new vaccine introduction [9, 12, 15, 17, 29]. The review by Zimet, *et al.* concluded that vaccine safety and cost were two critical factors for policymaker acceptance—conclusions supported by our findings [49].

Our results suggest that an effective advocacy strategy, in partnership with multiple internal and external stakeholders, is necessary to ensure successful HPV vaccine adoption in low-resource settings, a recommendation noted by others [15, 34]. An HPV vaccine advocacy strategy should include accurate information; multiple methods for dissemination, including workshops, mass media, and grassroots organizations; and strategic partnerships with key ministries and external stakeholders [14]. Our results confirm that formative research is a useful methodology to identify the information needs of policymakers in order to tailor advocacy messages that are most effective in addressing the specific information requested [15].

Finally, we note the conflicting statements made by many respondents related to the cost of HPV vaccines. Some remarked that the current vaccine price is unaffordable. Yet others observed that vaccine financing or procurement is possible through external support from international bodies, such as the GAVI Alliance (co-financing), UNICEF (procurement), or the Pan American Health Organization Revolving Fund (procurement for Latin America) [14]. It may be that policymakers are unable to speculate on projected costs for HPV vaccine introduction because, at this time, there is no known public sector pricing for the vaccine. National budgeting for the vaccine may also be difficult with the price of the vaccine still unknown. This may have caused some respondents to focus on the current price of the vaccine in developed-country markets rather than the final subsidized price that would eventually be borne by low-resource countries. Therefore, the recent news that the GAVI Alliance will consider HPV vaccines in their investment strategy for 2009-2013 [50] is encouraging. It may help to alleviate price concerns, which could accelerate the vaccine policy process for HPV within “early adopter” countries.

While our analysis provides valuable information about the policy process for HPV vaccine introduction in low-resource settings, there are some limitations to our results. First, the data analyzed for this study are the country-specific technical reports of the formative research rather than the transcripts of the in-depth interviews themselves. The analysis thus relied on the research teams' firsthand understanding of the data. Second, while an inductive process was used to analyze the data, it was difficult to distinguish whether missing data were not collected or just not considered important to include in the country reports. Third, our project countries were selected for their representativeness of their regions, burden of cervical cancer, health system infrastructure, and potential to adopt HPV vaccines, but they may not be fully representative of all policy processes in low-resource areas. Fourth, policymakers and policy influencers interviewed in our study were purposively sampled based on their government agency and position. Data were lacking as to the number of policymakers or policy influencers who might have been invited to participate in the study and refused (if any) and the reasons for refusals. Lastly, policy

processes are complex and can be heavily influenced by unanticipated political or social events. The experience of the next few years (especially as documented in the four project countries) will reveal the extent to which the processes described above drive decision-making on adoption of HPV vaccine.

CONCLUSION

Despite these limitations, the results of this study provide new insights into the policy process for HPV vaccine introduction among four low-resource countries. While results from this analysis were focused on the policy level of vaccine adoption, many policymakers indicated that factors related to the health system infrastructure would directly impact policy formulation, introduction, and implementation. These factors included sustainable financing for HPV vaccine implementation and concerns raised at the community or individual levels, such as mistrust in the vaccine's purposes and the safety of the vaccine. The expression of these concerns validated the use of a multilevel ecological framework for exploring the policy environment [30, 31]. The results from this study suggest that the critical steps and needs for HPV vaccine policy formulation and adoption in low-resource settings may be more similar than generally assumed. Understanding these similarities may assist other low-income countries in accelerating their policymaking processes for HPV vaccines.

ACKNOWLEDGMENTS

This research was funded by the Bill & Melinda Gates Foundation and coordinated by PATH, Seattle, Washington. We extend special gratitude to our colleagues, research partners, and study participants who contributed to the formative research studies in India, Peru, Uganda, and Vietnam. We also wish to thank Dr. Vivien Tsu for her insightful comments to drafts of this manuscript.

REFERENCES

- [1] Ferlay, J.; Bray, F.; Pisani, P.; Parkin, D.M. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide, IARC CancerBase No. 5, version 2.0. <http://www-dep.iarc.fr/globocan/database.htm> (accessed May 16, 2008).
- [2] Parkin, D.M.; Bray, F. Chapter 2: the burden of HPV-related cancers. *Vaccine*, **2006**, *24*(Suppl. 3), S11-S25.
- [3] Munoz, N.; Castellsague, X.; de Gonzalez, A.B.; Gissmann, L. Chapter 1: HPV in the etiology of human cancer. *Vaccine*, **2006**, *24*(Suppl. 3), S1-S10.
- [4] Denny, L.; Quinn, M.; Sankaranarayanan, R. Chapter 8: screening for cervical cancer in developing countries. *Vaccine*, **2006**, *24*(Suppl. 3), S71-S77.
- [5] World Health Organization (WHO). *Human Papillomavirus and HPV Vaccines: Technical Information for Policymakers and Health Professionals*; WHO: Geneva, **2007**.
- [6] Paavonen, J.; Jenkins, D.; Bosch, F.X.; Naud, P.; Salmeron, J.; Wheeler, C.M.; Chow, S.N.; Apter, D.L.; Kitchener, H.C.; Castellsague, X.; De Carvalho, N.S.; Skinner, S.R.; Harper, D.M.; Hedrick, J.A.; Jaisamram, U.; Limson, G.A.; Dionne, M.; Quint, W.; Spiessens, B.; Peeters, P.; Struyf, F.; Wieting, S.L.; Lehtinen, M.O.; Dubin, G. Efficacy of a prophylactic adjuvanted bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial. *Lancet*, **2007**, *369*(9580), 2161-2170.
- [7] Villa, L.L.; Costa, R.L.; Petta, C.A.; Andrade, R.P.; Paavonen, J.; Iversen, O.E.; Olsson, S.E.; Hoye, J.; Steinwall, M.; Riis-Johannessen, G.; Andersson-Ellstrom, A.; Elfren, K.; Krogh, G.; Lehtinen, M.; Malm, C.; Tamms, G.M.; Giacoletti, K.; Lupinacci, L.; Railkar, R.; Taddeo, F.J.; Bryan, J.; Esser, M.T.; Sings, H.L.; Saah, A.J.; Barr, E. High sustained efficacy of a prophylactic quadrivalent human papillomavirus types 6/11/16/18 L1 virus-like particle vaccine through 5 years of follow-up. *Br. J. Cancer*, **2006**, *95*(11), 1459-1466.
- [8] Clemens, J.D.; Jodar, L. Translational research to assist policy decisions about introducing new vaccines in developing countries. *J. Health Popul. Nutr.*, **2004**, *22*(3), 223-231.
- [9] Mahoney, R. Policy analysis: an essential research tool for the introduction of vaccines in developing countries. *J. Health Popul. Nutr.*, **2004**, *22*(3), 331-337.
- [10] DeRoeck, D.; Jodar, L.; Clemens, J. Putting typhoid vaccination on the global health agenda. *N. Engl. J. Med.*, **2007**, *357*(11), 1069-1071.
- [11] Sherris, J.; Agurto, I.; Arrossi, S.; Dzuba, I.; Gaffikin, L.; Herdman, C.; Limpaphayom, K.; Luciani, S. Advocating for cervical cancer prevention. *Int. J. Gynaecol. Obstet.*, **2005**, *89*(Suppl. 2), S46-S54.
- [12] Munira, S.L.; Fritzen, S.A. What influences government adoption of vaccines in developing countries? A policy process analysis. *Soc. Sci. Med.*, **2007**, *65*(8), 1751-1764.
- [13] Hanney, S.R.; Gonzalez-Block, M.A.; Buxton, M.J.; Kogan, M. The utilisation of health research in policy-making: concepts, examples and methods of assessment. *Health Res. Policy Syst.*, **2003**, *1*(1), 2.
- [14] International AIDS Vaccine Initiative (IAVI); PATH. *HPV Vaccine Adoption in Developing Countries: Cost and Financing Issues*; IAVI and PATH: New York, **2007**.
- [15] Sherris, J.; Friedman, A.; Wittet, S.; Davies, P.; Steben, M.; Saraiya, M. Chapter 25: education, training, and communication for HPV vaccines. *Vaccine*, **2006**, *24*(Suppl. 3), S210-S218.
- [16] WHO; United Nations Population Fund. *Preparing for the Introduction of HPV Vaccines: Policy and Programme Guidance for Countries*; WHO: Geneva, **2006**.
- [17] DeRoeck, D. The importance of engaging policymakers at the outset to guide research on and introduction of vaccines: the use of policymaker surveys. *J. Health Popul. Nutr.*, **2004**, *22*(3), 322-330.
- [18] Bingham, A.; Janmohamed, A.; Bartolini, R.; Creed-Kanashiro, H.; Katahoire, A.; Khan, I.; Lyazi, I.; Menezes, L.; Murokara, D.; Nguyen, N.; Tsu, V. An approach to formative research in HPV vaccine introduction planning in low-resource settings. *Open Vaccine J.*, **2009**, *2*, 1-16.
- [19] Green, L.W.; Kreuter, M.W. *Health Program Planning: An Educational and Ecological Approach*; McGraw-Hill: New York, **2005**.
- [20] Guest, G.; MacQueen, K.M. Reevaluating Guidelines in Qualitative Research. In *Handbook for Team-Based Qualitative Research*; Guest, G.; MacQueen, K. M.; Eds.; Altamira: Lanham, **2008**; pp. 205-226.
- [21] Menezes, L.; Jacob, M.; Gandhi, S.; Kaipilyawar, S.; Patki, M.; Bingham, A.; Wittet, S.; LaMontagne, D.S.; Mawar, N.; Paranjape, R.; Chaudry, K.; Tsu, V. Developing an evidence base for cervical cancer vaccine introduction, planning and implementation in India. *Indian J. Med. Res.*, **2009**, (In press).
- [22] Katahoire, A.; Jitta, J.; Kivumbi, G.; Murokora, D.; Arube Wani, J.; Siu, G.; Arinaitwe, L.; Bingham, A.; Mugisha, E.; Tsu, V.; LaMontagne, D.S. An assessment of the readiness for introduction of the HPV vaccine in Uganda. *Afr. J. Reprod. Health*, **2008**, *12*(3), 159-172.
- [23] PATH; National AIDS Research Institute (NARI). *Assessing Introduction of HPV Vaccine in India: Phase I Formative Study*; PATH and NARI: New Delhi, **2008**.
- [24] Instituto de Investigación Nutricional (IIN). *Strategies for the Introduction of the Human Papilloma Virus (HPV) Vaccine for the Prevention of Cervical Cancer: Formative-Qualitative Study*; IIN: Lima, **2007**.
- [25] IIN. *Study for the Introduction of HPV Vaccine in Peru, Activity 1: Mapping the National Immunization Strategy*; IIN: Lima, **2007**.
- [26] Katahoire, A.; Jitta, J.; Arube-Wani, J.; Kivumbi, G.; Murokora, D.; Siu, G.; Arinaitwe, L.; Lyazi, I. *Formative Research Report: An Assessment of the Readiness for Introduction of a Cervical Cancer Vaccine in Uganda*; Child Health and Development Centre: Kampala, **2008**.
- [27] PATH; National Institute of Hygiene and Epidemiology (NIHE). *Report on the Policy Environment for HPV Vaccine Introduction in Vietnam*; PATH and NIHE: Hanoi, **2008**.

- [28] NIHE; PATH. *Evaluation of the Health System and School Health Program for HPV Vaccine Introduction in Vietnam*; NIHE and PATH: Hanoi, **2008**.
- [29] Andrus, J.K.; Toscano, C.M.; Lewis, M.; Oliveira, L.; Roper, A.M.; Davila, M.; Fitzsimmons, J.W. A model for enhancing evidence-based capacity to make informed policy decisions on the introduction of new vaccines in the Americas: PAHO's ProVac initiative. *Public Health Rep.*, **2007**, *122*(6), 811-816.
- [30] Kaljee, L.M.; Pack, R.; Pach, A.; Nyamete, A.; Stanton, B.F. Sociobehavioural research methods for the introduction of vaccines in the diseases of the most impoverished programme. *J. Health Popul. Nutr.*, **2004**, *22*(3), 293-303.
- [31] Simpson, E.; Wittet, S.; Bonilla, J.; Gamazina, K.; Cooley, L.; Winkler, J.L. Use of formative research in developing a knowledge translation approach to rotavirus vaccine introduction in developing countries. *BMC Public Health*, **2007**, *7*(147), 281.
- [32] Stanton, B.F. Assessment of relevant cultural considerations is essential for the success of a vaccine. *J. Health Popul. Nutr.*, **2004**, *22*(3), 286-292.
- [33] Kingdon, J.W. *Agendas, Alternatives, and Public Policies*; Little, Brown and Company: Boston, **1984**.
- [34] Sabatier, P.; Jenkins-Smith, H. The Advocacy Coalition Framework: An Assessment. In *Theories of the Policy Process*; Sabatier, P., Ed.; Westview Press: Boulder, **1999**; pp. 117-168.
- [35] Grindle, M.S.; Thomas, J.W. *Public Choices and Policy Change: The Political Economy of Reform in Developing Countries*; Johns Hopkins Press: Baltimore, **1991**.
- [36] Hyder, A.A.; Bloom, G.; Leach, M.; Syed, S.B.; Peters, D.H. Exploring health systems research and its influence on policy processes in low income countries. *BMC Public Health*, **2007**, *7*, 309.
- [37] Stetler, C.B.; Ritchie, J.; Rycroft-Malone, J.; Schultz, A.; Charns, M. Improving quality of care through routine, successful implementation of evidence-based practice at the bedside: an organizational case study protocol using the Pettigrew and Whipp model of strategic change. *Implement. Sci.*, **2007**, *2*, 3.
- [38] Gonzalez-Block, M.A. Health policy and systems research agendas in developing countries. *Health Res. Policy Syst.*, **2004**, *2*(1), 6.
- [39] Arrossi S.; Sankaranarayanan R.; Parkin D.M. Incidence and mortality of cervical cancer in Latin America. *Salud Publica Mex.*, **2003**, *45*(Suppl. 3), S306-S314.
- [40] National Cancer Registry Programme, Indian Council of Medical Research (ICMR). *An Assessment of the Burden and Care of Cancer Patients: Consolidated Report of Hospital Based Cancer Registries 2001-2003*; National Cancer Registry Programme, ICMR: Bangalore, **2007**.
- [41] National Cancer Registry Programme, ICMR. *Incidence and Distribution of Cancer: Consolidated Report of Population-Based Cancer Registries 2001-2004*; National Cancer Registry Programme, ICMR: Bangalore, **2006**.
- [42] Nandagudi, S.; Chaudhry, K.; Saxena, S. Trends in cervical cancer incidence-Indian scenario. *Eur. J. Cancer Prev.*, **2005**, *14*(6), 513-518.
- [43] Denny, L.; Quinn, M.; Sankaranarayanan, R. Chapter 8: screening for cervical cancer in developing countries. *Vaccine*, **2006**, *24* (Suppl. 3), S71-S77.
- [44] WHO. The WHO Prequalification Project. <http://www.who.int/mediacentre/factsheets/fs278/en/index.html> (accessed May 16, 2008).
- [45] Gilson, L.; Raphaely, N. The terrain of health policy analysis in low and middle income countries: a review of published literature 1994-2007. *Health Policy Plan.*, **2008**, *23*(5), 294-307.
- [46] Bingham A.; Drake J.K.; LaMontagne D.S. Sociocultural issues in the introduction of human papillomavirus vaccines in low-resource settings. *Arch. Pediatr. Adolesc. Med.*, **2009**, *163*(5), 455-461.
- [47] Shiffman, J. Generating political priority for maternal mortality reduction in five developing countries. *Am. J. Public Health*, **2007**, *97*(5), 796-803.
- [48] WHO. Meeting of the immunization Strategic Advisory Group of Experts, November 2008—conclusions and recommendations. *Wkly. Epidemiol. Rec.*, **2009**, *84*(1/2), 1-16.
- [49] Zimet, G.D.; Liddon, N.; Rosenthal, S.L.; Lazcano-Ponce, E.; Allen, B. Chapter 24: psychosocial aspects of vaccine acceptability. *Vaccine*, **2006**, *24*(Suppl. 3), S201-S209.
- [50] GAVI Alliance. *Vaccine Investment Strategy*; GAVI Alliance: Washington, DC, **2008**.

Received: February 20, 2009

Revised: June 29, 2009

Accepted: June 29, 2009

© Program for Appropriate Technology in Health (PATH) ; Licensee *Bentham Open*.This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.