



## Acceptability of multipurpose human papillomavirus vaccines among providers and mothers of adolescent girls: A mixed-methods study in five countries



Nadja A. Vielot<sup>a,\*</sup>, Shoshana K. Goldberg<sup>a</sup>, Gregory Zimet<sup>b</sup>, Sara B. Smith<sup>a</sup>, Mary Anne McDonald<sup>c</sup>, Silvina Ramos<sup>d</sup>, Karen Morgan<sup>e,f</sup>, Chan Joo Kim<sup>g</sup>, Karin L. Richter<sup>h</sup>, Merce Peris<sup>i</sup>, Kevin J. Whaley<sup>j</sup>, Jennifer S. Smith<sup>a,k</sup>

<sup>a</sup> Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, 135 Dauer Drive, 2101 McGavran-Greenberg Hall, CB# 7435, Chapel Hill, NC 27599, USA

<sup>b</sup> Section of Adolescent Medicine, Indiana University School of Medicine, Indianapolis, IN, USA

<sup>c</sup> Center on Genomics, Race, Identity, Difference (GRID), Duke University, Durham, NC, USA

<sup>d</sup> Centro de Estudios de Estado y Sociedad, Buenos Aires, Argentina

<sup>e</sup> Perdana University, Royal College of Surgeons in Ireland School of Medicine, Kuala Lumpur, Malaysia

<sup>f</sup> Royal College of Surgeons in Ireland, Dublin, Ireland, UK

<sup>g</sup> Department of Obstetrics and Gynecology, The Catholic University of Korea, Medical College, St Paul's Hospital, Seoul, Korea

<sup>h</sup> Department of Medical Virology, University of Pretoria and National Health Laboratory Services, Pretoria, South Africa

<sup>i</sup> Unit of Infections and Cancer, Cancer Epidemiology Research Programme, Institut Català d'Oncologia, Barcelona, Spain

<sup>j</sup> Mapp Biopharmaceutical, Inc., San Diego, CA, USA

<sup>k</sup> UNC Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA

### ARTICLE INFO

#### Keywords:

Vaccines  
Acceptability  
Multipurpose  
Human papillomavirus  
Sexually transmitted infections  
Adolescents

### ABSTRACT

**Introduction:** Multipurpose vaccines (MPVs) could be formulated to prevent multiple sexually transmitted infections simultaneously. Little is known about acceptability of MPVs among vaccine health care providers (HCPs) or mothers of adolescent girls.

**Methods:** 151 adolescent vaccine providers and 118 mothers of adolescent girls aged 9–14 were recruited from five geographically-diverse countries: Argentina, Malaysia, South Africa, South Korea, and Spain. We assessed providers' preferences for single-purpose human papillomavirus (HPV) vaccine versus MPVs (including HPV +herpes simplex virus (HSV)-2, HPV+HIV, or HPV+HSV-2+HIV) via quantitative surveys. Maternal MPV attitudes were assessed in four focus group discussions (FGDs) in each country.

**Results:** Most providers preferred MPVs over single-purpose HPV vaccination, with preference ranging from 61% in Malaysia to 96% in South Africa. HPV+HSV-2+HIV was the most preferred MPV formulation (56–82%). Overall, 53% of the mothers preferred MPVs over single-purpose HPV vaccines, with strongest support in South Africa (90%) and lowest support in South Korea (29%). Convenience and trust in the health care system were commonly-cited reasons for MPV acceptability. Safety and efficacy concerns were common barriers to accepting MPVs, though specific concerns differed by country. Across FGDs, additional safety and efficacy information on MPVs were requested, particularly from trusted sources like HCPs.

**Conclusions:** Though maternal acceptability of MPVs varied by country, MPV acceptability would be enhanced by having HCPs provide parents with additional MPV vaccine safety and efficacy information. While most providers preferred MPVs, future health behavior research should identify acceptability barriers, and targeted provider interventions should equip providers to improve vaccination discussions with parents.

**Abbreviations:** FGD, focus group discussion; HCP, health care provider; HIV, human immunodeficiency virus; HPV, human papilloma virus; HSV, herpes simplex virus; MPV, multipurpose vaccine; STI, sexually transmitted infections

\* Corresponding author.

E-mail address: [nadjavielot@unc.edu](mailto:nadjavielot@unc.edu) (N.A. Vielot).

<http://dx.doi.org/10.1016/j.pvr.2017.04.001>

Received 27 November 2016; Received in revised form 26 March 2017; Accepted 1 April 2017

Available online 06 April 2017

2405-8521/ © 2017 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Sexually-transmitted infections (STIs) can have severe long-term effects on sexual and reproductive health. Herpes simplex virus (HSV-2) and human immunodeficiency virus (HIV) contribute to high global morbidity, and cannot be cured or prevented by prophylactic vaccination. Research on HSV-2 and HIV preventive technologies is underway, and the Multipurpose Technology Working Group has prioritized the development of technologies to prevent both infections simultaneously [1]. We therefore posit that multipurpose technologies could be effective for STI/HIV prevention in adolescents, conferring STI/HIV protection before sexual debut.

Prophylactic multipurpose vaccines (MPVs) could reduce acceptability and adherence barriers to STI/HIV prevention. One of the first MPVs was licensed in the United States in 1948 against diphtheria, tetanus, and pertussis [2]. By 2015, diphtheria-tetanus-acellular pertussis (Tdap) vaccination exceeded 80% in the United States, largely controlling these high-morbidity infections and demonstrating that MPVs can be acceptable to caregivers [3].

Human papillomavirus (HPV) is one of the only vaccine-preventable STIs. HPV vaccines are highly-efficacious against high-grade cervical lesions – which are associated with cervical, vaginal, vulvar, and anal cancers – caused by high-risk HPV types [4]. Given the high global priority of preventing HPV-associated cancers, HPV vaccines were licensed in over 100 countries and integrated into 87 countries' national vaccination programs by November 2016 [5]. HPV vaccines could serve as the basis for an MPV to prevent multiple STIs, including HSV-2 and HIV.

To date, no such MPVs have been developed, nor have any published studies explored the acceptability of MPVs for STIs/HIV. It remains unknown whether providers would administer MPVs, or whether parents of adolescents would accept them, presenting a potential barrier to future MPV program implementation.

To assess the acceptability of hypothetical MPVs for STI/HIV prevention, we conducted a mixed-methods study among adolescent vaccine providers and mothers of adolescent girls in five geographically-diverse countries. We hypothesized that MPV preference would be high among providers [6–12] and mixed among mothers, based on barriers reported in the HPV vaccine literature [13–17]. To our knowledge, this is the first study to assess providers' and mothers' attitudes toward MPVs, providing insight into the acceptability of MPVs as a strategy to promote sexual health in adolescents.

## 2. Methods

### 2.1. Study participants

#### 2.1.1. Providers (Quantitative)

Providers from Argentina, Malaysia, South Africa, South Korea and Spain were identified via non-probability convenience sampling and recruited through mail, email, phone, or in-person. Eligible providers were authorized to administer adolescent vaccines per each country's medical regulations.

#### 2.1.2. Mothers (Qualitative)

Between November 2013 and April 2014, each country conducted four focus group discussions (FGDs). Mothers were recruited using non-probability convenience sampling from medical offices, health centers, or schools. Eligible mothers had a daughter old enough to receive HPV vaccination, based on each country's vaccination guidelines at the time of data collection (minimum age: South Africa=9; Argentina/South Korea/Spain=11; Malaysia=13). Participating mothers were assigned to FGDs based on whether their daughters had received HPV vaccination. In Spain, six mothers of unvaccinated daughters completed in-depth interviews rather than FGDs. To ensure comparability of the findings across countries, this analysis reports findings from FGDs only.

In-country institutional review boards (IRB) approved this study prior to data collection. University of North Carolina (UNC) study staff received IRB approval for analysis of de-identified secondary data.

### 2.2. Measures

#### 2.2.1. Providers (Quantitative)

Providers' demographic information and attitudes towards single-purpose HPV vaccine and MPVs were collected by a study interviewer trained in structured interviewing techniques. Two questions assessed MPV attitudes: 1) "MPVs in the future may protect against HPV plus other infections, such as HSV-2 or HIV. Which would you prefer to recommend to girls and their parents: A vaccine for HPV alone, or an MPV?"; 2) "If an MPV were available, which would you be most likely to recommend: HPV +HSV-2; HPV+ HIV; or HPV+HSV-2+HIV?" Providers were allowed to answer "No preference" or "Would not recommend MPV".

#### 2.2.2. Mothers (Qualitative)

Each FGD followed a semi-structured discussion guide that assessed mothers' attitudes towards various aspects of adolescent HPV vaccination; the present analysis involves discussions around MPVs. Discussion moderators gave prompts from the discussion guide, and additional questions emerged through probing and clarifying statements (Appendix A). Although HPV vaccines are approved for girls and boys, this study focused on vaccination for girls in keeping with local HPV vaccination recommendations [18–21].

### 2.3. Analysis

#### 2.3.1. Providers (Quantitative)

In-country staff double-entered de-identified data into English language EpiData forms, and translated data into English when necessary. Data were cleaned and analyzed at UNC, the central coordinating site. Univariate tabulations were performed in SAS 9.4 (SAS Institute Inc., Cary, NC).

#### 2.3.2. Mothers (Qualitative)

In-country researchers facilitated the verbatim transcription of FDG recordings and their translation to English. Translations were reviewed by in-country study staff who were native speakers of the language used in the FDGs and fluent in English. UNC study staff reviewed the translations for meaning, and clarified colloquial usages, local references, and cultural contexts with the lead in-country researchers before analysis, and during analysis as needed.

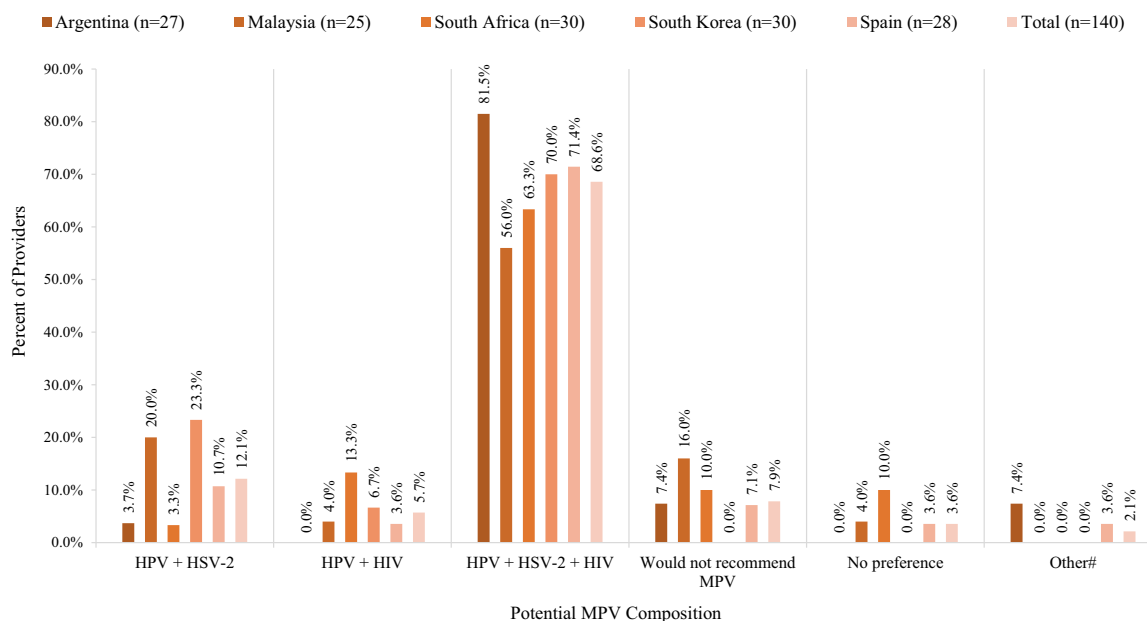
Cleaned transcripts were entered into ATLAS.ti (ver. 7, Berlin, Germany) for thematic content coding. An experienced qualitative researcher supervised data management and analysis. An initial codebook was developed based on themes outlined in the FGD script, and additional codes were added iteratively as they emerged from the data [22]. One transcript from each country was reviewed and coded independently by two research assistants using initial and additional codes; coded transcripts were then compared, and inconsistent coding decisions were discussed and reconciled [23]. Additional codes were incorporated into the existing codebook, and remaining transcripts were coded using the same procedure. Qualitative data are summarized by commonly-cited themes.

## 3. Results

### 3.1. Providers (Quantitative analysis)

#### 3.1.1. Providers' medical practices

Of 353 providers contacted, 151 were enrolled between October 2013 and April 2014 across the five countries (Argentina [n=30]; Malaysia [n=30]; South Africa [n=31]; South Korea [n=30]; and Spain [n=30]). Providers were primarily family physicians and general practitioners (31.1%), obstetrician-gynecologists (25.8%), and pedia-



**Fig. 1.** Providers' preferences for multipurpose vaccine composition in five countries (n=140). Providers reported their preferred MPV composition from the options listed in the chart, and were given the opportunity to suggest alternative vaccine components.

\*11 providers did not provide a response to this question.

#One provider from Spain preferred HSV-2+HIV only. Two providers from Argentina did not suggest alternative components, but expressed general hesitance to recommend MPVs.

tricians (21.9%) who provided vaccine services principally in clinics (80.1%) and private facilities (53.6%) (Table A1).

All providers from Argentina (100%), and most from Spain (86.7%) and Malaysia (76.7%), had ever provided HPV vaccine to adolescents, compared with half in South Korea (50.0%) and one-third in South Africa (35.5%) (Table A2). Overall, most (57.4%) providers preferred to administer HPV vaccine concomitantly with other vaccines (e.g., hepatitis A/B, influenza, tetanus-diphtheria-pertussis), though preference for concomitant administration varied across countries (> 75% in Argentina and Spain vs. 16.0% in South Korea) (Table A2).

### 3.1.2. Providers' attitudes towards MPVs

Providers' preference for MPVs over single-purpose HPV vaccine was high (82.3% overall), from 60.7% in Malaysia to 96.0% in South Africa. Among 107 providers who preferred MPVs, a formulation including HPV, HSV-2, and HIV was the most highly-preferred (56.0–81.5%) in all countries (Fig. 1). One Spanish provider preferred vaccination against HSV-2+HIV only (3.6%), and two Argentinian providers hesitated to recommend MPVs in general (7.4%).

## 3.2. Mothers (Qualitative analysis)

### 3.2.1. Mothers' overall attitudes towards MPVs

A total of 118 mothers (70 with vaccinated daughters, 48 with unvaccinated daughters) were enrolled across five countries (Argentina [n=23]; Malaysia [n=26]; South Africa [n=21]; South Korea [n=31]; and Spain [n=17]), with a median 5.5 participants per group. Malaysian mothers had the highest proportion of vaccinated daughters (80.7%), and South Korea had the lowest proportion (25.8%) (Table A1). Half of mothers (52.5%, n=62) stated a preference for MPVs; MPV preference was highest in South Africa (90.5%, n=19) and lowest in South Korea (29.0%, n=8) (Table A3). MPV support was slightly higher among mothers of vaccinated girls (55.7%, n=39) than unvaccinated girls (47.9%, n=23), though notable differences emerged by country (Table A3). In South Korea and Malaysia, MPV support was higher among mothers of vaccinated girls than unvaccinated girls, (South Korea: 37.5% [3/8] vs. 26.1% [6/23]; Malaysia: 71.4% [15/21] vs. 0.0% [0/5]), whereas in Argentina and South Africa, mothers of unvaccinated girls were more likely to support MPVs over single-

purpose vaccines (Argentina: 47.1% [8/17] vs. 50.0% [3/6]; South Africa: 71.4% [5/7] vs. 100% [14/14]).

Mothers' perceived advantages and disadvantages of MPVs emerged from the FGDs along several cross-country themes, detailed below. We also observed variation in MPV perceptions by country (Table A3).

### 3.2.2. Perceived advantages of MPVs

**3.2.2.1. Convenience.** Across all countries, 23 mothers (n=11 [15.7%] vaccinated; n=12 [25%] unvaccinated) perceived MPVs to be more convenient than single-purpose vaccines. Mothers noted that it was "good to just get it over with at once" (South Korea, unvaccinated), and appreciated that with "one shot, it is finished" (Malaysia, vaccinated). Others framed convenience in terms of health benefits, preferring MPVs for conferring "two for one" (Spain, vaccinated) multi-disease immunity and their ability to "kill ten-thousand birds with one stone" (Argentina, vaccinated).

**3.2.2.2. Addresses teenage risk.** Eighteen mothers (n=14 [20%] vaccinated; n=4 [8.3%] unvaccinated) reported that MPVs would protect their adolescent daughters once they inevitably engaged in sexual behavior.

"[Sex] is one thing that we cannot stop our kids from doing...They like experimenting...So at least if they can be protected, why not [vaccinate]?" (South Africa, vaccinated).

**3.2.2.3. Trust in vaccine development.** Eleven mothers (n=7 [10%] vaccinated; n=4 [8.3%] unvaccinated) across all countries trusted pharmaceutical companies to develop safe and effective vaccines, believing that they "probably have done some research somewhere and are sure of immunity up to this point" (South Africa, vaccinated). Confidence in vaccine development often translated to general comfort with vaccines. One mother was unconcerned with potential side effects, as "studies are done at a national level and it is decided that there is a high enough number of cases to determine [support for] a vaccine." (Spain, vaccinated).

### 3.2.3. Perceived barriers to MPVs

**3.2.3.1. Side effects.** Fear of potential MPV side effects was the most commonly-reported concern (n=12 [17.1%] vaccinated; n=14 [29.2%] unvaccinated), often described in non-specific language: “side effects”; “something bad.” Mothers of unvaccinated girls were generally more concerned about side effects:

*“I’m hesitating because of the side effects but there isn’t any information on that.”* (South Korea, unvaccinated).

Conversely, mothers of vaccinated girls viewed side effects as just one piece of information needed: *‘It’s also interesting to know about the side effects, if there are any.’* (Argentina, vaccinated).

**3.2.3.2. Strength of the vaccine.** Across all countries, 15 mothers (n=11 [15.7%] vaccinated; n=4 [8.3%] unvaccinated) expressed concern that combining multiple vaccines would make MPVs too strong to be safe. These mothers felt that MPVs were “too much for just one time” (Argentina, vaccinated), increasing the risk of side effects. Conversely, 12 mothers (10 [14.3%] vaccinated; 2 [4.2%] unvaccinated) mothers feared that MPVs would be weaker than a single-purpose vaccine, believing that they would be either too non-specific to have an effect, or would not be fully-efficacious against all infections:

*It being a general vaccine, is it really going to be protecting the child?* (South Africa, vaccinated).

*Multipurpose doesn’t concentrate on one kind. The effect of each [vaccine] can be mixed, diluted, or toxic when you use all together. It’s like having 70% for each rather than 90% for one....* (South Korea, unvaccinated).

**3.2.3.3. Mistrust of pharmaceutical companies.** Seven mothers (n=3 [4.3%] vaccinated; n=4 [8.3%] unvaccinated) in Argentina, Malaysia, and South Korea cited mistrust in the pharmaceutical industry, believing that they had “economic interests there” (Argentina, vaccinated). Mothers also suspected that pharmaceutical companies wanted to experiment on their daughters, that MPVs would be of poor quality, or that MPVs would be developed for provider/pharmaceutical convenience rather than for health benefits.

### 3.2.4. Information needed to accept MPVs

When probed on the additional information they would need to accept MPVs, mothers requested information along several major themes.

**Safety information**, such as anticipated side effects, was most commonly requested: *“If it’s preventive and more clinical results and side effects become clear, then I’ll consider it”* (South Korea, unvaccinated). This led nine (9) mothers across three countries to prefer to “wait and see” (Malaysia, unvaccinated) how others responded to MPVs, and/or for MPV uptake to become more widespread, before accepting MPVs.

**Process information** included logistical issues such as the target population, vaccination requirements, and who would administer vaccines:

*... I don’t know if it is going to be done in all the areas and all the regions...with the 9–14 [year olds]. I would prefer that [MPVs] be taken over all the schools.* (South Africa, vaccinated).

**Vaccination literacy** reflected low perceived health knowledge. These mothers were confused about HPV infection and the concept of MPVs: *“What is papillomavirus, then why does it affect the uterus?”* (Spain, vaccinated); *“It’s too scientific. Like I don’t understand the word multivalent”* (Argentina, unvaccinated). Many mothers called for widespread information dissemination through “media...or television”,

*“drug company...brochures”, or “talks at school, for the parents and the kids”* to increase their vaccine literacy.

Most commonly, mothers desired information from a trusted source to make a final decision. For these mothers, the established relationship with “the family doctor in your area, the one you go to, who knows you” (Argentina, unvaccinated) instilled a unique trust in their providers:

*I don’t trust everything on the internet, so everybody still needs to find that family [general practitioner] that you trust, just to check....* (Malaysia, vaccinated).

Others were less concerned with the source, desiring only that information come from trustworthy “public associations...say, Ministry of Health.” (South Korea, unvaccinated).

## 4. Discussion

This mixed-methods study demonstrated acceptability of MPVs to protect against HPV and STIs/HIV among providers in five countries. Most providers preferred MPVs to HPV vaccination alone, and providers also expressed the strongest preference for an MPV that prevents multiple STIs (HPV, HSV-2, and HIV). MPV support was lower among mothers than providers; half of mothers preferred MPVs to single purpose vaccines, though notable variation emerged by country and daughter’s vaccination status.

Mothers who preferred MPVs cited convenience, a need for STI prevention, and confidence in the safety and efficacy of approved vaccines. Yet, support for MPVs among some mothers was tentative, even among those who preferred them to single-purpose HPV vaccines. Mothers from all countries expressed potential concerns, including the efficacy of individual vaccine components; increased side effects; reticence to accept a new drug; and suspicion of pharmaceutical companies. Concerns regarding safety and overloading of the immune system are consistent with findings from research on parental attitudes toward existing combination childhood vaccines, such as measles-mumps-rubella and Tdap [24,25].

Evidence from the HPV vaccine literature may help explain lower maternal MPV acceptability, as well as between-country differences in MPV acceptability. Provider and maternal preference for MPVs was highest in South Africa (96% and 91%, respectively), reflecting high HPV vaccine acceptability by providers in prior studies in Sub-Saharan Africa [26,27]. In a qualitative study of HPV vaccine acceptability among 39 adolescent-caregiver dyads in Soweto, South Africa, mothers considered HPV vaccination a solution to a perceived inability to protect their daughters from STIs [28]. Mothers also discussed the importance of STI/HPV prevention given South Africa’s HIV epidemic [28], paralleling themes that emerged in our own sample. Conversely, MPV support was lower in South Korea (29%) than in all other countries. In this study, South Korean mothers were unique in citing financial barriers to MPV acceptability, potentially because a nationally-funded HPV vaccination program did not exist at the time of data collection; this program began June 2016 [29,30]. Previous studies of HPV vaccine acceptability among South Korean adults and mothers have consistently found that cost was a barrier to HPV vaccine acceptability [31–33], suggesting that future vaccination programs address the financial implications of MPVs.

A limitation of this study is the focus on MPV acceptability without assessing acceptability of individual HIV and HSV-2 vaccines. However, prior studies have shown acceptability of HIV and HSV-2 vaccines from providers, policy-makers, and community members globally [34–38]. This study also focused on vaccination in girls, based on the countries’ HPV vaccination recommendations at the time of data collection. While gender-neutral vaccination policies can protect boys from STIs and harmful sequelae, and prevent transmission to girls, low- and middle-income countries tend to prioritize vaccination in girls to maximize the cost-effectiveness of HPV vaccination [39]. Small sample sizes of providers and mothers limit the generalizability of the findings within study countries, and preclude the use of statistical tests



to assess group differences between mothers of vaccinated and unvaccinated daughters. Convenience sampling of mothers similarly limits generalizability; mothers were recruited primarily from urban settings, and may not represent the diverse populations of their countries. Further, the interview guide contained more prompts regarding MPV concerns than advantages. Thus, it is unclear if the many reports of concerns reflect true discomfort with MPVs, or are simply the result of heavy focus on concerns in the FGDs. Finally, some mothers did not actively participate in discussions, resulting in low response rates to certain prompts.

Findings from this mixed-methods study offer key information to guide the development and roll-out of future MPVs. Our inclusion of five geographically-diverse countries furthers understanding of similarities and differences in MPV perceptions across cultures. Including mothers of vaccinated and unvaccinated girls offers perspectives on local patterns of HPV vaccination that may be considered in developing future MPV programs. By including both providers and mothers, we triangulated vaccination attitudes and potential acceptability barriers from the two sources most influential in adolescent vaccination. Regardless of vaccine preference, mothers desired additional information from a known health-care provider about side effects and efficacy before accepting MPVs. This corroborates findings from prior studies indicating that a provider's recommendation is the most important predictor of adolescent vaccination, and emphasizes the need to intervene with providers and caregivers to promote adolescent vaccination [40,41].

### 5. Conclusions

Providers and mothers of adolescent girls reported generally high

acceptability of hypothetical MPVs to prevent STIs/HIV, provided that safety and efficacy are demonstrated in clinical trials. Educating healthcare providers on concise, effective approaches to MPV communication could enhance acceptability of potentially life-saving vaccines. Near-term research should develop culturally-tailored information about emerging MPVs that anticipates and addresses caregivers' concerns. Global financial and political commitment will be needed to develop and promote MPVs, particularly to vulnerable populations in resource-limited settings.

### Funding sources

This study was an ancillary study to the GlaxoSmithKline (GSK) Biologicals SA funded parent study (ID: 117339) which aimed to compare two versus three dose HPV vaccination. GSK was not involved in the conduct and analysis of this ancillary study. GSK was provided the opportunity to review this manuscript for accuracy but the authors are solely responsible for final content and interpretation.

Nadja A. Vielot was supported by the National Institute of Allergy and Infectious Diseases Training in Infectious Diseases Epidemiology grant during the completion of this work (#5T32AI070114).

### Acknowledgements

Clare Barrington, PhD, Associate Professor of Health Behavior at UNC, provided guidance on qualitative analysis methods.

## Appendix A. Discussion guide for multipurpose vaccine acceptability among mothers of adolescent girls

[Discussion leader reads].

“Multipurpose vaccines protect against more than one type of infection or illness. Researchers are working on new multipurpose vaccines against HPV plus another infection. Some of these multipurpose HPV vaccines protect against HPV plus illnesses like Herpes, which can cause sores in the genital area; Hepatitis B, which can cause liver damage; or HIV, which causes the immune system to stop working.

“What do you think about a multipurpose HPV vaccine?”

Follow-up questions:

- (If daughter is currently unvaccinated against HPV) Which would you prefer for your daughter: a vaccine for HPV alone or a multipurpose vaccine?
- (If daughter is currently vaccinated against HPV) If you had another daughter who was not yet vaccinated, which would you prefer: a vaccine for HPV alone or a multipurpose vaccine?
- What are some reasons for this?
- Which other infections would you want this vaccine to protect your daughter against?
- Do you have any concerns or worries about a multipurpose HPV vaccine?
- If so, what concerns or worries do you have?
- What kind of information would you need to help you to feel less worried about a multipurpose vaccine?

See Appendix Tables A1–A3.

**Table A1**

Descriptive characteristics of adolescent vaccine providers and mothers of daughters in five countries.

	Adolescent vaccine providers (n=151)					Overall (n = 151)
	Argentina (n = 30)	Malaysia (n = 30)	South Africa (n = 31)	South Korea (n = 30)	Spain (n = 30)	
<b>Dates of interviews</b>	Feb-Mar 2014	Nov-Dec 2013	Feb-Mar 2014	Nov 2013-Jan 2014	Dec 2013-Apr 2014	Nov 2013-Apr 2014
<b>Provider catchment area</b>	San Luis Province Olivos and Vicente López <sup>a</sup> City of Rosario <sup>b</sup>	Putrajaya <sup>c</sup> Selangor state	Pretoria Mamelodi	Seoul Incheon	Hospitalet de Llobregat <sup>c</sup> Granollers <sup>c</sup> Sabadell <sup>c</sup> Llavaneres <sup>c</sup>	–

(continued on next page)

Table A1 (continued)

	Adolescent vaccine providers (n=151)					
	Argentina (n = 30)	Malaysia (n = 30)	South Africa (n = 31)	South Korea (n = 30)	Spain (n = 30)	Overall (n = 151)
<b>Dates of interviews</b>	Feb-Mar 2014	Nov-Dec 2013	Feb-Mar 2014	Nov 2013-Jan 2014	Dec 2013-Apr 2014	Nov 2013-Apr 2014
	City of San Lorenzo <sup>b</sup>			Bundang, Bucheon	Esplugues de Llobregat <sup>c</sup>	
	City of San Genaro <sup>b</sup>	Kuala Lumpur <sup>c</sup>	Atteridgeville <sup>d</sup>	Reus <sup>f</sup>	Cerdanyola <sup>e</sup>	
	Ilsan			Gerona	City of Buenos Aires	
	La Pobl de Segur <sup>h</sup>			Puigcerdà <sup>g</sup>		
<b>Type of provider</b>						
Family/internal medicine, general practice	5 (16.7%)	26 (86.7%)	8 (25.8%)	6 (20%)	2 (6.6%)	47 (31.1%)
Midwife	–	–	2 (6.5%)	–	7 (23.3%)	9 (6%)
Nurse/nurse practitioner	–	3 (10.0%)	10 (32.3%)	–	4 (13.3%)	17 (11.3%)
OB/GYN	12 (40.0%)	2 (6.7%)	7 (22.6%)	12 (40%)	6 (20%)	39 (25.8%)
Pediatrician	13 (43.3%)	1 (3.3%)	–	12 (40%)	7 (23.3%)	33 (21.9%)
Pharmacist	–	–	2 (6.5%)	–	–	2 (1.3%)
Preventive physician	–	–	–	–	4 (13.3%)	4 (2.6%)
Health promoter	–	–	2 (6.5%)	–	–	2 (1.3%)
<b>Place of vaccine provision</b>						
Clinic	25 (83.3%)	28 (93.3%)	16 (51.6%)	28 (93.3%)	24 (80%)	121 (80.1%)
School	–	1 (3.3%)	5 (16.1%)	–	3 (10%)	9 (6.0%)
Hospital	12 (40.0%)	1 (3.3%)	15 (48.4%)	2 (6.7%)	8 (26.7%)	38 (25.2%)
Health NGO/Pharmacy	–	–	2 (6.45%)	–	–	2 (1.3%)
<b>Type of vaccine provision</b>						
Public only	4 (13%)	–	17 (54.8%)	–	22 (73.3%)	43 (28.5%)
Private only	11 (36.7%)	28 (93.3%)	11 (35.5%)	30 (100%)	1 (3.3%)	81 (53.6%)
Both	15 (50.0%)	1 (3.3%)	3 (9.7%)	–	7 (23.3%)	26 (17.2%)
<b>Mothers of daughters (n=118)</b>	Argentina (n = 23)	Malaysia (n = 26)	South Africa (n = 21)	South Korea (n = 31)	Spain (n = 23)	Overall (n = 118)
<b>Date</b>	Feb-Mar 2014	Jan-Apr 2014	Nov-Dec 2013	Dec 2013-Jan 2014	Dec 2013-Apr 2014	Nov 2013-Apr 2014
<b>Location</b>						
-FGD 1	Buenos Aires (n=5)	Kuala Lumpur (n=5)	Atteridgeville (n=6)	Seoul (n=8)	Barcelona (n=6)	
-FGD 2	San Isidro <sup>a</sup> (n=7)	Kuala Lumpur (n=11)	Kwaggasrand <sup>d</sup> (n=4)	Seoul (n=8)	Sabadell (n=5)	
-FGD 3	San Isidro <sup>a</sup> (n=6)	Johor Bahru (n=5)	Prinshof (n=3) <sup>i</sup>	Seoul (n=8)	Montcada (n=4)	
-FGD 4	Vicente López <sup>a</sup> (n=5)	Selangor (n=5)	Kwaggasrand (n=8) <sup>i</sup>	Gyeonggi-do (n=7)	Mataró (n=2)	
<b>Daughters vaccinated against HPV</b>	17 (73.9%)	21 (80.7%)	7 (33.3%)	8 (25.8%)	17 (73.9%)	70 (59.3%)
<b>Daughters unvaccinated against HPV</b>	6 (26.1%)	5 (19.2%)	14 (66.7%)	23 (74.2%)	6 (26.1%) <sup>j</sup>	48 (40.7%)

OB/GYN=obstetrician/gynecologist; FGD=focus group discussion; HPV=human papillomavirus

<sup>a</sup> Buenos Aires Province;

<sup>b</sup> Santa Fe Province;

<sup>c</sup> Wilayah;

<sup>d</sup> township outside of Pretoria;

<sup>e</sup> Barcelona Province;

<sup>f</sup> Tarragona Province;

<sup>g</sup> Gerona Province;

<sup>h</sup> Lérida Province;

Table A2

Adolescent vaccine practices and attitudes among providers in five countries.

Country	Ever provided HPV vaccine to adolescents 9–14 years		Preference for concomitant administration of HPV and other adolescent vaccines <sup>a</sup>		Preference for MPVs over single-purpose HPV vaccine	
	N	n (%)	N	n (%)	N	N (%)
Argentina	30	30 (100.0%)	26	20 (76.9%)	24	22 (91.7%)
Malaysia	30	23 (76.7%)	27	15 (55.6%)	28	17 (60.7%)
South Africa	31	11 (35.5%)	24	14 (58.3%)	25	24 (96.0%)
South Korea	30	15 (50.0%)	25	4 (16.0%)	28	22 (78.6%)
Spain	30	26 (86.7%)	27	21 (77.8%)	25	22 (88.0%)
<b>Total<sup>b</sup></b>	<b>151</b>	<b>105 (69.5%)</b>	<b>129</b>	<b>74 (57.4%)</b>	<b>130</b>	<b>107 (82.3%)</b>

<sup>a</sup> Including meningococcal, tetanus-diphtheria-pertussis, influenza, and Hepatitis A/B.

<sup>b</sup> Denominator for preference questions does not add to 151 owing to missing/invalid responses (N=22 missing responses for concomitant administration; N=21 missing responses for MPV preference)

**Table A3** Emergent themes related to multi-purpose vaccination from focus group discussions, stratified by country.

	Argentina	Malaysia	South Africa	South Korea	Spain
<b>Preferred vaccine administration</b>					
MPV	11 (47.8%)	15 (57.7%)	19 (90.5%)	9 (29.0%)	8 (47.1%)
Single purpose	6 (26.1%)	2 (7.7%)	2 (9.5%)	11 (35.5%)	3 (17.7%)
Unknown	6 (26.1%)	9 (42.9%)	0 (0.0%)	11 (35.5%)	6 (35.3%)
<b>Support for MPV</b>	Preventing multiple diseases at once	Only mothers of vaccinated daughters expressed preference for MPV	Praised ability of MPV to address perceived teenage sexual risk	Support was relatively low, and mostly took a 'wait and see' approach	Acceptance of MPVs was contingent on safety and efficacy evidence, and was generally low
<b>Barriers to MPV</b>	Belief that daughters had low HPV/STI risk at their current ages. Concern that MPV was too strong to be safe or too broad to be effective.	MPV acceptance was conditional on safety and efficacy evidence.	Inrequent concerns, mostly related to potential efficacy of MPV.	Potential high cost of MPVs. Belief that daughters had low HPV/STI risk at their current ages.	MPV acceptance was conditional on safety and efficacy evidence.
<b>Other emergent themes</b>	Mothers in all groups believed that MPV efficacy would be lower than single vaccine efficacy.	Strong willingness to accept recommendations from trusted sources (namely providers such as their family physician) before accepting MPV.	Most enthusiasm for MPVs of all countries, with very few concerns reported for side effects or lack of efficacy.	Concern that MPV would be a pharmaceutical ploy for financial gain.	Lowest health knowledge around HPV vaccination. Most likely to request basic information on vaccines before accepting MPVs. Strong desire for safety and efficacy information to make a decision, given low knowledge of the existing HPV vaccine.

**References**

- [1] A. Hemmerling, P. Harrison, B. Y. Holt, J. Manning, A. Stone, and K. J. Whaley, "Multipurpose prevention technologies for reproductive health: Advancing the scientific and product development agenda," 2011.
- [2] Immunization Action Coalition, Historic Dates and Events Related to Vaccines and Immunization. [Online]. Available: (<http://www.immunize.org/timeline/>). (accessed 05-Dec-2015), 2015.
- [3] World Health Organization, WHO vaccine-preventable diseases: monitoring system global summary, 2016. [Online]. Available: ([http://apps.who.int/immunization\\_monitoring/globalsummary/incidences?C=USA](http://apps.who.int/immunization_monitoring/globalsummary/incidences?C=USA)). (accessed 02-Oct-2016), 2016.
- [4] Merck & Co. Inc, HPV-related cancers and diseases. [Online]. Available: (<https://www.gardasil9.com/hpv-facts/related-cancer-diseases/>). (accessed 04-Oct-2016), 2016.
- [5] Cervical Cancer Action, Global Progress in HPV Vaccination., 2016.
- [6] I. Lataifeh, N. Obeidat, L. Al-Mehaisen, W. Khriesat, R. Tadros, Y. Khader, S. Al-Sukhun, A survey of Jordanian obstetricians and gynecologists' knowledge and attitudes toward human papillomavirus infection and vaccination, *Eur. J. Gynaecol. Oncol.* 35 (4) (2014) 429–432.
- [7] B. Audu, M. Bukar, A. Ibrahim, T. Swende, Awareness and perception of human papilloma virus vaccine among healthcare professionals in Nigeria, *J. Obstet. Gynaecol. (Lahore)*. 34 (8) (2014) 714–717.
- [8] C. Lasset, J. Kalecinski, V. Régnier, G. Barone, Y. Leocmach, P. Vanhems, F. Chauvin, D. Lutringer-Magnin, Practices and opinions regarding HPV vaccination among French general practitioners: evaluation through two cross-sectional studies in 2007 and 2010, *Int. J. Public Health* 59 (3) (2014) 519–528.
- [9] A. Mazzadi, M. Paolino, S. Arrossi, Aceptabilidad y conocimientos sobre la vacunacion contra el virus del papiloma humano (VPH) en medicos ginecologos de la Argentina, *Salud Publica Mex.* 54 (5) (2012) 515–522.
- [10] P. Remes, V. Selestine, J. Changalucha, D.A. Ross, D. Wight, S. de Sanjosé, S. Kapiga, R.J. Hayes, D. Watson-Jones, A qualitative study of HPV vaccine acceptability among health workers, teachers, parents, female pupils, and religious leaders in northwest Tanzania, *Vaccine* 30 (36) (2012) 5363–5367.
- [11] C.C. Makwe, R.I. Anorlu, Knowledge of and attitude toward human papillomavirus infection and vaccines among female nurses at a tertiary hospital in Nigeria, *Int. J. Women's. Health* 3 (1) (2011) 313–317.
- [12] D. Lutringer-Magnin, J. Kalecinski, G. Barone, Y. Leocmach, V. Regnier, A.C. Jacquard, B. Soubeyrand, P. Vanhems, F. Chauvin, C. Lasset, Human papillomavirus (HPV) vaccination: perception and practice among French general practitioners in the year since licensing, *Vaccine* 29 (32) (2011) 5322–5328.
- [13] A.L. Friedman, K.O. Oruko, M.A. Habel, J. Ford, J. Kinsey, F. Odhiambo, P.A. Phillips-Howard, S.A. Wang, T. Collins, K.F. Laserson, E.F. Dunne, Preparing for human papillomavirus vaccine introduction in Kenya: implications from focus-group and interview discussions with caregivers and opinion leaders in Western Kenya, *BMC Public Health* 14 (1) (2014) 855.
- [14] A.G. Ramirez, N.S. Weiss, A.E.C. Holden, L. Suarez, S.P. Cooper, E. Munoz, S.L. Naylor, Incidence and risk factors for hepatocellular carcinoma in Texas Latinos: implications for prevention research, *PLoS One* 7 (4) (2012).
- [15] C. Wiesner, M. Piñeros, L. Trujillo, C. Cortés, Aceptabilidad de la vacuna contra el virus papiloma humano en padres de adolescentes, en Colombia, *Rev. Salud Pública* 12 (6) (2010) 961–973.
- [16] P. Paul, A.E. Tanner, P.E. Gravitt, K. Vijayaraghavan, K.V. Shah, G.D. Zimet, Acceptability of HPV vaccine implementation among parents in India, *Heal. Care Women Int* 35 (10) (2014) 1148–1161.
- [17] J.K. Cover, N.Q. Nghi, D.S. LaMontagne, D.T.T. Huyen, N.T. Hien, L.T. Nga, Acceptance patterns and decision-making for human papillomavirus vaccination among parents in Vietnam: an in-depth qualitative study post-vaccination, *BMC Public Health* 12 (1) (2012) 629.
- [18] K. Richter, "Implementation of HPV vaccination in South Africa," 2015.
- [19] S.W.P. Ezat, R. Hod, J. Mustafa, A.Z. Hatta, M. Dali, A.S. Sulaiman, A. Azman, National HPV immunisation programme: knowledge and acceptance of mothers attending an obstetrics clinic at a teaching hospital, Kuala Lumpur, *Asian Pac. J. Cancer Prev.* 14 (5) (2013) 2991–2999.
- [20] European Centre for Disease Prevention and Control, Vaccine Schedule. [Online]. Available: (<http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx>). (accessed 09-Feb-2017), 2017.
- [21] H. Patel, E. Wilson, C. Vizzotti, G. Parston, J. Prestt, A. Darzi, Argentina's successful implementation of a national human papillomavirus vaccination Program, *Health Aff.* 35 (2) (2016) 301–308.
- [22] K.M. MacQueen, Codebook development for team-based qualitative analysis, *Field Methods* 10 (2) (1998) 31–36.
- [23] M. Miles, A. Huberman, J. Saldana, *Qualitative Data Analysis: A Methods Sourcebook*, 3rd ed, Sage Publications, Inc, Thousand Oaks, CA, 2014.
- [24] S. Hilton, M. Pettecirow, K. Hunt, Combined vaccines are like a sudden onslaught to the body's immune system: parental concerns about vaccine 'overload' and 'immune-vulnerability', *Vaccine* 24 (20) (2006) 4321–4327.
- [25] K.F. Brown, J.S. Kroll, M.J. Hudson, M. Ramsay, J. Green, S.J. Long, C.A. Vincent, G. Fraser, N. Sevdalis, Factors underlying parental decisions about combination childhood vaccinations including MMR: a systematic review, *Vaccine* 28 (26) (2010) 4235–4248.
- [26] M.S. Cunningham, C. Davison, K.J. Aronson, HPV vaccine acceptability in Africa: a systematic review, *Prev. Med.* 69 (2014) 274–279.
- [27] S. Perlman, R.G. Wamai, P.A. Bain, T. Welty, E. Welty, G. Ogumbo, Knowledge and awareness of HPV vaccine and acceptability to vaccinate in Sub-Saharan Africa: a systematic review, *PLoS One* 9 (3) (2014).

- [28] I.T. Katz, B. Nkala, J. Dietrich, M. Wallace, L. Bekker, K. Pollenz, L.M. Bogart, A.A. Wright, A.C. Tsai, D.R. Bangsberg, G.E. Gray, A qualitative analysis of factors influencing HPV vaccine uptake in Soweto, South Africa among adolescents and their caregivers, *PLoS One* 8 (8) (2013).
- [29] WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre), *Human Papillomavirus and Related Diseases Report: Korea, Republic of Summary Report*, 2014.
- [30] M. Son, J. Yun, Cancer mortality projections in Korea up to 2032, *J. Korean Med. Sci.* 31 (2016) 892–901.
- [31] J. Oh, M. Kyung, E.H. Yun, E. Lee, H. Shin, Awareness of and attitude towards human papillomavirus infection and vaccination for cervical cancer prevention among adult males and females in Korea: a nationwide interview survey, *Vaccine* 28 (2010) 1854–1860.
- [32] H.S. Kang, L. Moneyham, Attitudes, intentions, and perceived barriers to human papillomavirus vaccination among Korean high school girls and their mothers, *Cancer Nurs.* 34 (3) (2011) 202–208.
- [33] J. Kim, H. Kang, Mothers' knowledge, health beliefs and intentions to vaccinate their daughters against human papillomavirus in Korea, *Contemp. Nurs.* 47 (1) (2014) 97–107.
- [34] E.A. Williams, D.J.M. Lewis, S. Bertholet, M. Zazzi, Anticipating policy considerations for a future HIV vaccine: a preliminary study, *Vaccine* 34 (2016) 3697–3701.
- [35] L.H. Abdullahi, B.M. Kagina, T. Cassidy, E.F. Adebayo, C.S. Wiysonge, G.D. Hussey, Knowledge, attitudes and practices on adolescent vaccination among adolescents, parents and teachers in Africa: a systematic review, *Vaccine* 34 (2016) 3950–3960.
- [36] L.M. McClarty, R.R. Lorway, S. Ramanaik, J. Wylie, M.L. Becker, Factors influencing frontline health service providers' likelihood to recommend a future, preventive HIV vaccine to key populations in Karnataka, south India, *Vaccine* 33 (2015) 656–663.
- [37] M.B. Short, S.L. Rosenthal, Fostering acceptance of human papillomavirus and herpes simplex virus vaccines among adolescents and parents, *Curr. Opin. Pediatr.* 18 (2006) 53–57.
- [38] G.D. Zimet, S.M. Perkins, L.A. Sturm, R.M. Bair, B.E. Juliar, R.M. Mays, Predictors of STI vaccine acceptability among parents and their adolescent children, *J. Adolesc. Heal.* 37 (2005) 179–186.
- [39] M. Jit, C. Levin, M. Brisson, A. Levin, S. Resch, J. Berkhof, J. Kim, R. Hutubessy, Economic analyses to support decisions about HPV vaccination in low- and middle-income countries: a consensus report and guide for analysts, *BMC Med.* 11 (23) (2013).
- [40] G.D. Zimet, Health care professionals and adolescent vaccination: a call for intervention research, *Hum. Vaccin. Immunother.* 10 (9) (2014) 2629–2630.
- [41] T.G. Hopkins, N. Wood, Female human papillomavirus (HPV) vaccination: global uptake and the impact of attitudes, *Vaccine* 31 (13) (2013) 1673–1679.