

**PERSUASIVE MESSAGING FOR HUMAN PAPILLOMAVIRUS VACCINATION BY
ADOLESCENT PROVIDERS IN A FIVE COUNTRY MULTI-SITE STUDY**

Janvier Rwamwejo MD, MSPH, IBCLC¹, Silvina Ramos², Karen Morgan, PhD, MA³, Karin Richter, MBChB, FCPATH, MMed⁴, Chan Joo Kim, MD⁵, Mercè Peris, MD, MPH⁶, and Jennifer S. Smith, PhD, MPH^{1,7}

¹Department of Epidemiology, UNC Gillings School of Global Public Health, Chapel Hill, NC, USA

²Centro de Estudios de Estado y Sociedad, Buenos Aires, Argentina

³Perdana University- Royal College of Surgeons in Ireland School of Medicine, Malaysia

⁴Department of Medical Virology, University of Pretoria, National Health Laboratory Service Pretoria, South Africa

⁵Department of Obstetrics and Gynecology, The Catholic University of Korea, College OF Medicine, St Paul's Hospital, Seoul, South Korea

⁶Unit of Infections and Cancer, Cancer Epidemiology Research Programme, Institut Catala d'Oncologia, Barcelona, Spain

⁷Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA

Corresponding Author:

Jennifer S. Smith, PhD MPH, Professor, Department of Epidemiology
University of North Carolina at Chapel Hill
Gillings School of Global Public Health
2103 McGavran-Greenberg Hall
Campus Box# 7435 Chapel Hill, NC 27599-7435
(P) 919.966.7450 (C) 919.593.4091 (F) 919.966.2089
jennifers@unc.edu

Article Highlights:

Providers' primary message to motivate parents to vaccinate daughters against HPV was cervical cancer prevention.

Television was cited as main source of information, followed by one-on-one discussions, and information at school.

Pediatricians and OB/GYNs more frequently preferred messages focusing specifically on cervical cancer prevention.

Author Disclosure:

This study was an ancillary study to the GlaxoSmithKline 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. Janvier Rwamwejo was supported by the University of North Carolina's Graduate School Doctoral Merit Assistantship for study in Epidemiology during the completion of this work.

ABSTRACT

Objective: Strong persuasive messaging by providers is a key predictor for patient acceptance of prophylactic human papillomavirus (HPV) vaccination. We aimed to determine optimal messaging to promote HPV adolescent vaccination across different geographical sites.

Methods: Adolescent providers (n=151) from Argentina, Malaysia, South Africa, South Korea, and Spain were surveyed on messages, family decision makers and sources of communication to best motivate parents to vaccinate their adolescent daughters overall, and against HPV.

Multivariate logistic regression assessed likelihood of recommending messages specifically targeted at cervical cancer with providers' characteristics: gender, medical specialization, and previous administration of HPV vaccination.

Results: Mothers were considered the most important HPV vaccination decision makers for their daughters (range 93%-100%). Television was cited as the best source of information on HPV vaccination in surveyed countries (range 56.5-87.1%), except Spain where one-on-one discussions were most common (73.3%). Prevention messages were considered the most likely to motivate parents to vaccinate their daughters overall; and against HPV, in all five countries (range 30.8-55.9%). Optimal messages emphasized cervical cancer prevention, and included strong provider recommendation to vaccinate, vaccine safety and efficacy, timely vaccination, and national policy for HPV vaccination. Pediatricians and obstetricians/ gynecologists were more likely to cite that the best prevention messages should focus on cervical cancer (OR: 4.2, 95% CI: 1.17-15.02 versus other medical specialists).

Conclusions: Provider communication messages that would motivate parents to vaccinate against HPV were based on strong recommendation emphasizing prevention of cervical cancer. To frame convincing messages to increase vaccination uptake, adolescent providers should receive updated training on HPV and associated cancers, while clearly addressing HPV vaccination safety and efficacy.

Key words: cervical cancer, human papillomavirus, vaccination, messaging, multi-site study

Article precis:

Strong provider recommendations to prevent cervical cancer were optimal to motivate parents to vaccinate against HPV.

INTRODUCTION

Invasive cervical cancer (ICC) is the fourth most common cancer in women worldwide¹ and is caused by high-risk (oncogenic) types of human papillomavirus (hrHPV) infection².

Approximately 260,000 women die each year from ICC globally, of which 87% occur in low-resource settings³. HrHPV types can cause other HPV-associated cancers, including vaginal, vulvar, anal, penile, and oropharyngeal cancers⁴.

Three highly effective prophylactic vaccines⁵ are available for the prevention of HPV-associated cancers; the nonavalent vaccine is projected to prevent ~90% of cervical cancers, 80-85% of vaginal cancers and of vulvar cancers; ~85 of penile cancers, and ~90-95% of anal/rectal cancers in vaccinated women and men⁶.

Current World Health Organization (WHO) guidelines recommend routine immunization of adolescent girls 9 to 14 years of age in most national vaccination programs globally, via provision in schools, healthcare facilities, and/or community-based setting⁷. Despite the overwhelming evidence concerning the safety and efficacy of HPV vaccination, uptake among young adolescent girls, the primary target population, remains relatively low in several regions of the world⁸.

Efforts to increase the uptake of HPV vaccination involve the effective engagement of key stakeholders, including health providers, policy makers, parents and their adolescent children, as

well as community and religious leaders, teachers, and the media⁹. Nevertheless, the key element known to increase patient uptake of HPV vaccination is the strong recommendation by healthcare providers for HPV vaccination¹⁰. Positive public messaging concerning cervical cancer, HPV infection, and HPV vaccination can also improve population-based acceptability of HPV vaccination¹¹.

Given the key role of providers' recommendations on the uptake of HPV vaccination, it is critical to further understand providers' attitudes about optimal messaging, sources of messaging information, and to whom messages should be conveyed to inform future HPV vaccination roll-out in countries. Although communication strategies to increase vaccination among adolescent girls have been previously evaluated¹², very few studies have directly compared adolescent health care providers' attitudes towards optimal messages to motivate parents to obtain HPV vaccination for adolescent girls across different geographical sites¹³. Recommended messages of trusted health professionals are particularly timely and important in the context of negative media messaging campaigns in different geographical areas worldwide.¹⁴

To address this gap in the literature, we present results here on providers' attitudes on optimal messaging/communication strategies to increase HPV vaccination uptake from a multi-site study conducted in five countries: Argentina, Malaysia, Spain, South Africa, and South Korea.

METHODS

Study participants

Providers from five countries were identified via non-probability convenience sampling, and recruited through mail, email, phone, or in-person. Providers were eligible if they were authorized to administer adolescent vaccines according to each country's medical regulations.

Of a total of 353 providers contacted, 151 providers were enrolled between October 2013 and April 2014: Argentina (n=30); Malaysia (n=30); South Africa (n=31); South Korea (n=30); and Spain (n=30). Institutional review board (IRB) approval was obtained from all collaborating institutions prior to data collection. The University of North Carolina at Chapel Hill (UNC-CH) received IRB approval for analysis of de-identified secondary data.

Measures

A quantitative survey assessing demographics and descriptive information was administered to each adolescent provider by a study interviewer trained in structured interviewing techniques. The survey assessed providers' attitudes about persuasive messages to increase the acceptability and uptake of adolescent vaccination. Four questions were specifically addressed to adolescent vaccine providers: 1. "In your experience, what messages best work to motivate parents to vaccinate their adolescent daughters?" 2. "What messages would motivate parents to vaccinate their daughters against human papillomavirus (HPV)?" 3. "Which family member or members are the most important in deciding whether a girl will be vaccinated against HPV?" 4. "What type of information sources are the most useful to reach parents with information about the HPV vaccine?" Given that these four questions elicited open-ended responses, providers gave a narrative recorded by the interviewer.

Statistical Analysis

In-country staff entered the data twice (double-entered data) in English language Epi Data forms without personal identifiers and translated data into English where necessary. Data were cleaned and analyzed at the UNC-CH, Gillings School of Global Public Health. Univariate tabulations were performed in R 3.5.0. statistical software¹⁵, and data comparison between countries was analyzed using the Fisher's exact test, an alternative to the Chi Square test¹⁶. Multivariable

logistic regression models were used to assess associations between three providers' characteristics (gender, medical field, and previous administration of HPV vaccination) and providers' citing that cervical cancer targeted-messaging would motivate parents to vaccinate their daughters against human papillomavirus (HPV) as compared to other types of messaging.

RESULTS

Characteristics of Surveyed Providers

The most common medical specialty was family medicine (28.5%), followed by obstetricians-gynecologists (OB/GYNs) (23.2%), pediatricians (23.2%), with the remainder being nurse practitioners (9.9%), midwives (6.6%), pharmacists (1.9%), internal medicine physicians (1.4%) or other provider types (5.3%). All providers from Argentina (100%), most from Spain (86.7%) and Malaysia (76.7%) had provided HPV vaccination to adolescents, as compared with a half in South Korea (50%), and a third in South Africa (35.5%). Median years of practice per provider was 17.2 years overall, with some variation between countries (range: 13 years of practice in South Africa to 22 years in Spain).

Decision Making for HPV Vaccination

Mothers were consistently considered the most important decision makers for their daughters being vaccinated against HPV in all participating countries, ranging from 93.3% in Malaysia to 100% in Argentina and Spain. Fathers were the second most commonly reported decision makers: ranging from 10% in Malaysia to 61.3% in South Africa. Grandmothers and daughters were also reported to play a decision-making role in South Africa (41.9% and 45.2%, respectively) and Argentina (13.3% and 6.7%), but were not cited in other countries (Table 1).

Table 1: Family Members' Role in HPV Vaccine Decision Taking and Information Sources from 151 Adolescent Providers in a Five-Country Study

	Country						
	Argentina (n = 30)	Malaysia (n =30)	South Africa (n=31)	South Korea (n=30)	Spain (n=30)	Overall (n=151)	p value Fisher
“Which family member is the most important in deciding whether a girl will be vaccinated against HPV?”							
Type of Family Member							
Mothers	30 (100%)	28 (93.3%)	29 (93.5%)	29 (96.6%)	30 (100%)	146 (96.6%)	0.57
Fathers	6 (20%)	3 (10%)	19 (61.3%)	0 (0%)	6 (20%)	34 (22.5%)	<0.05
Grandmothers	4 (13.3%)	0 (0%)	13 (41.9%)	0 (0%)	0 (0%)	17 (11.2%)	<0.05
Daughters	2 (6.7%)	0 (0%)	14 (45.2%)	0 (0%)	0 (0%)	16 (10.6%)	<0.05
“What types of information sources are the most useful to reach parents with information about HPV vaccine?”							
Information Source							
Television	17 (56.6%)	17 (56.6%)	27 (87.1%)	21 (70%)	11 (36.6%)	93 (61.6%)	0.37
One-on-one-discussions	12 (40%)	11 (36.6%)	21 (67.7%)	7 (23.3%)	22 (73.3%)	73 (48.3 %)	<0.05
Info handed out at school	7 (23.3%)	9 (30%)	22 (71%)	13 (43.3%)	6 (20%)	57 (37.7 %)	0.12
Flyers	9 (30%)	13 (43.3%)	23 (74.2%)	1 (3.3%)	7 (23.3%)	53 (35.1%)	<0.05
Social media	5 (16.6%)	5 (16.6%)	18 (58.1%)	4 (13.3%)	6 (20%)	51 (33.7 %)	<0.05
Websites	5 (16.6%)	5 (16.6%)	23 (74.2%)	4 (13.3%)	9 (30%)	46 (30.5%)	<0.05
Posters and brochures	0 (0%)	15 (50 %)	25 (80.6%)	5 (16.6%)	1 (3.3%)	46 (30.5 %)	<0.05
Radio	1 (3.3%)	2 (6.6%)	12 (38.7%)	0 (0%)	1 (3.3%)	16 (10.6 %)	<0.05
Newspapers/newsletters	0 (0%)	0 (0%)	3 (9.7%)	1 (3.3%)	0 (0 %)	4 (2.6%)	0.09
Word-of-mouth	1 (3.3%)	0 (0%)	0 (0%)	2 (6.6%)	0 (0 %)	3 (1.9 %)	0.86

Information Sources

Television was considered the most effective source of information for HPV vaccination (Table 1). The prominent role of television was most notable in South Africa (87.1%) and South Korea (70%), and somewhat lower in Argentina and Malaysia (both at 56.6%), and Spain (36.6%). Spain was an exception in which "one-on-one-discussions" were the first chosen source of information, cited by 73.3% of surveyed Spanish providers. Likewise, one-on-one-discussions were also of notable importance in Argentina (40%). Posters and brochures was the second option in South Africa (80.6%) and Malaysia (50%), whereas in South Korea, information handed out at school was a second choice (43.3%). Of note, radio was less commonly recommended, overall by 10.6% of providers. Newspapers/newsletters (2.6%) and word-of-mouth (1.9%) were also rarely mentioned by providers (Table 1).

Best Messages Motivating Parents to Vaccinate their Daughters

In response to the question "What messages best work to motivate parents to vaccinate their daughters?", providers most commonly referred to non-specific messages about prevention against disease (39.7%), ranging from 21.9% in South Africa to 48.7 % in South Korea (Table 2). These messages "about prevention" included general statements about vaccination such as "Vaccination protects against serious diseases and death".

Types of Messages Motivating Parents to Vaccinate their Daughters against HPV

When asked the question specifically focused on HPV vaccination: "What messages would motivate parents to vaccinate their daughters against human papillomavirus (HPV)?", providers most commonly cited prevention messages with greater focus on HPV (48.7%), ranging from 30.8% in South Africa and 55.9 % in Spain (Table 2). Overall, the message that seemed to motivate parents the most to vaccinate their daughters against HPV was, by far, cervical cancer

Table 2: Messages Motivating Parents to Vaccinate Their Adolescent Daughters from 151 Providers in a Five- Country Study

	Country						
	Argentina (n = 30)	Malaysia (n = 30)	S. Africa (n = 31)	S. Korea (n = 30)	Spain (n = 30)	Overall (n = 151)	p value Fisher
“What messages best work to motivate parents to vaccinate their daughters?”							
Messages about Prevention	17 (48.5%)	15 (42.9 %)	9 (21.9%)	19(48.7%)	19 (38.8%)	79 (39.7%)	0.56
Recommendations from Providers	8 (22.9%)	5 (14.3%)	6 (14.6%)	12(30.8%)	5 (10.2%)	36 (18.1%)	0.47
Education/Awareness/Mass media	5 (14.3%)	11 (31.4%)	6 (14.6%)	0 (0%)	5 (10.2%)	27 (13.6%)	<0.05
Information about Vaccine Benefits	5 (14.3%)	0 (0%)	12 (29.3%)	1 (2.6%)	9 (18.3%)	27 (13.6%)	<0.05
Information about Vaccine Safety/Efficacy	0 (0 %)	4 (11.4%)	7 (17.1%)	2 (5.1%)	10 (20.4%)	23 (11.5%)	<0.39
Low vaccine cost	0 (0%)	0 (0%)	1 (2.5%)	5 (12.8%)	1 (2.1%)	7 (3.5%)	0.47
“What messages would motivate parents to vaccinate their daughters against human papillomavirus (HPV)?”							
Messages about Prevention	20 (51.2%)	18 (54.5%)	12 (30.8%)	33(50%)	24 (55.8%)	107 (48.7%)	0.60
HPV Vaccine Safety/Efficacy	0 (0%)	4 (12.1%)	2 (5.1%)	14(21.2%)	6 (13.9%)	26 (11.9%)	0.29
Education/Awareness/Mass media	9 (23.1%)	6 (18.1%)	6 (15.4%)	1(1.5%)	1 (2.4 %)	23 (10.5%)	<0.05
HPV Vaccine Benefits	1 (2.6%)	1 (3.1%)	10 (25.6%)	1(1.5%)	3 (6.9%)	16 (7.3%)	0.14
Provider recommendation for vaccination	5 (12.8%)	2 (6 %)	3 (7.7%)	2 (3%)	4 (9.3%)	16 (7.3%)	0.70
Timely vaccination	0 (0%)	0 (0%)	3 (7.7%)	7 (10.6%)	0 (0%)	10 (4.5%)	<0.05
Low vaccine cost	1 (2.6%)	1 (3.1%)	3 (7.7%)	3 (4.6%)	0 (0%)	8 (3.6%)	0.42
Recommendation about health policy*	3 (7.7%)	1 (3.1%)	0 (0%)	2 (3%)	1 (2.4%)	7 (3.1%)	0.30
Parental/collective responsibility	0 (0%)	0 (0%)	0 (0%)	3 (4.6%)	4 (9.3%)	7 (3.1%)	<0.05
“What types of prevention messages best work to motivate parents to vaccinate their daughters against HPV?”							
Prevention against cervical cancer	10 (50%)	3 (16.7 %)	4 (33.3%)	22(67.7%)	16 (66.6%)	55 (51.4%)	0.30
Prevention–only message	4 (20%)	13 (72.2%)	2 (16.7%)	0 (0%)	0 (0%)	19 (17.8%)	<0.05
Prevention against cancer/death	2 (10%)	2 (11.1%)	3 (25%)	3 (9%)	6 (25%)	16 (15%)	1
Prevention against HPV/ infection	3 (15%)	0 (0%)	2 (16.7%)	3 (9%)	1 (4.2%)	9 (8.4%)	0.41
Prevention against STIs	1 (5 %)	0 (0%)	0 (0%)	2 (6.1%)	1 (4.2%)	4 (3.8%)	0.69
Prevention against condylomas	0 (0%)	0 (0%)	1 (8.3%)	1 (3.1%)	1 (2.1%)	2 (1.8%)	0.81
Prevention against female diseases	0 (0%)	0 (0%)	0 (0%)	2 (6.1%)	0 (0%)	2 (1.8%)	0.64

*Includes messages: make vaccination mandatory/required/recommended (n=5); need of governmental approval(n=2).

prevention (51.4% overall; ranging from 16.7% in Malaysia to 66.7% in South Korea; $p = 0.30$). Other messages such as prevention of cancer or death (15%); HPV and infections (8.4%); sexually transmitted infections (STIs) (3.8%); condylomas (1.8%); and female diseases (1.8%) were less often cited. Prevention-only messages (messages which mentioned the term “prevention” without additional specification) were less frequently cited (17.8%). Messages included narratives such as “HPV vaccine is effective in preventing infections but it's not a cure” or “To raise awareness about HPV, Pap smear and colposcopy. To give more information on cervical cancer”. Some surveyed providers also recommended on time HPV vaccination using statements such as “The sooner you get vaccinated, the less chances of you being exposed to an infection”. Others reported verbatim: “Let’s protect our children from cervical cancer with a vaccination” or “Get immunized according to policies of health” (Table 2).

Most pediatricians, OB/GYNs, and midwives cited prevention messaging focused on cervical cancer as the most motivating message, while family physicians and nurse practitioners believed that the messages of prevention of cervical cancer and prevention against cancer death had similar success (Fig. 1). Some family physicians, midwives, and OB/GYNs (<20%) found that messages focused on HPV infection prevention and STIs prevention were good motivators. Pediatricians and OB/GYNs were more likely than other providers to provide a specific cervical cancer-targeted message (OR: 4.2, 95% CI:1.17-15.02; Table 3). Providers’ gender or having previously administered HPV vaccination was not associated with the likelihood of recommending specific cervical cancer-targeted messaging (Table 3).

Figure 1: Themes of Targeted Messaging to Increase HPV Vaccination among Adolescent Providers in 5 Countries

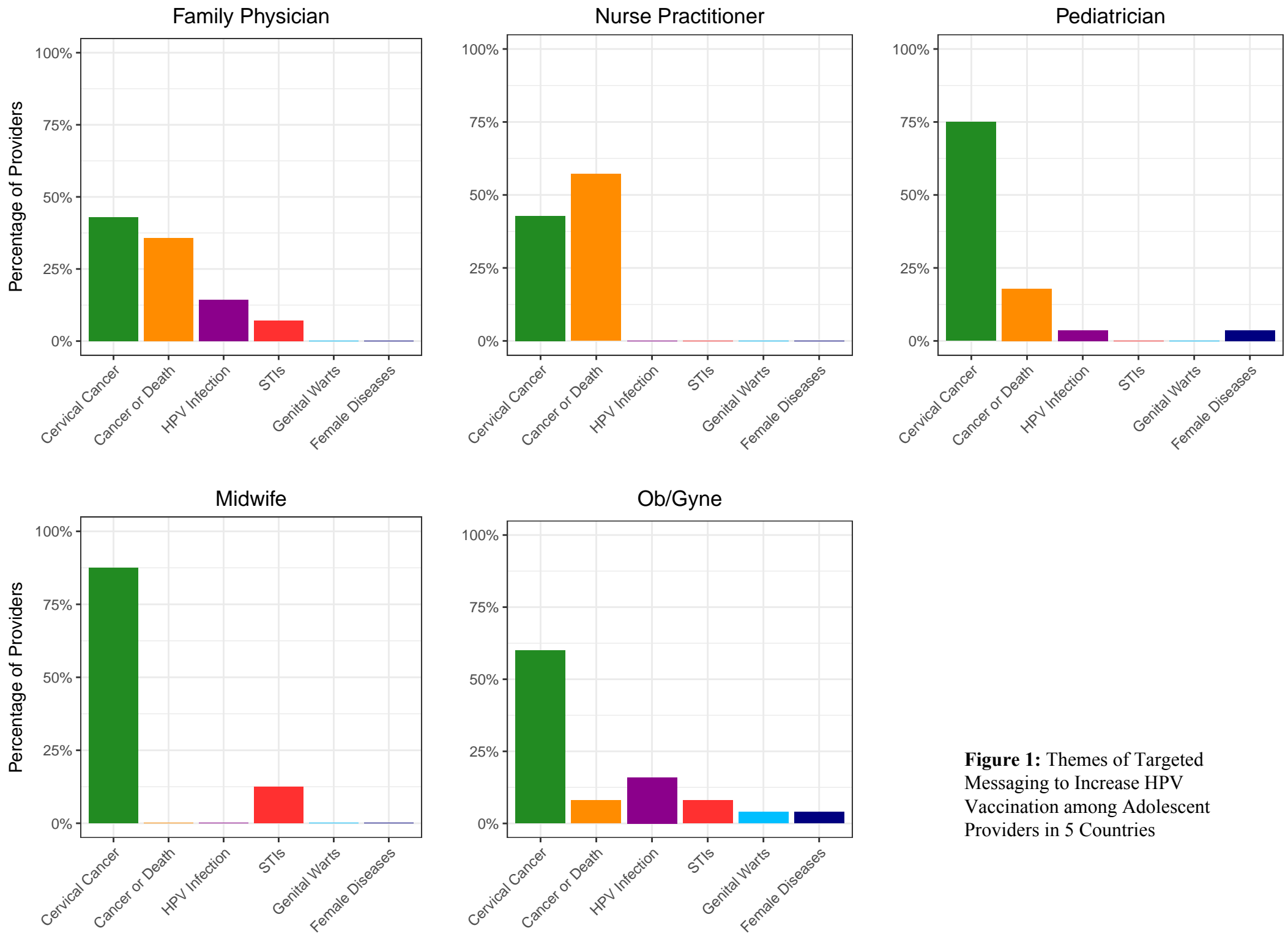


Figure 1: Themes of Targeted Messaging to Increase HPV Vaccination among Adolescent Providers in 5 Countries

Table 3: Predictors of Adolescent Vaccine Providers Using Cervical Cancer Prevention Messaging in a Five-Country Study

	Country					Multivariable Regression Estimates		
Provider's Characteristics	Argentina (n=30)	Malaysia (n=30)	S. Africa (n=31)	S Korea (n=30)	Spain (n=30)	Providers citing Cervical Cancer Prevention Messaging (%)	OR	95% CI
Pediatricians (n=35) or Obstetricians Gynecologists (n=35)								
Yes	25	2	6	25	12	65.5	4.2	(1.17-15.02)
No*	5	28	25	5	18	34.5	REF	
Provider Gender								
Male	19	9	22	13	22	52.7	1.65	(0.64-3.30)
Female	11	20	9	17	8	47.3	REF	
Administered HPV Vaccination								
Yes	30	23	11	15	26	69.1	1.11	(0.33-3.95)
No	0	7	20	15	4	30.9	REF	

OR=odds ratio; CI= confidence interval; REF=reference; *Includes Family Medicine Physicians (n=43); Nurse Practitioners (n=15); Midwives (n=10); Pharmacists (n=3); Internal Medicine Physicians (n=2) and Others (n=8).

DISCUSSION

This multi-center survey of providers of HPV vaccination conducted in five countries found that mothers were consistently considered the most influential family member when deciding whether to have their adolescent daughters vaccinated against HPV. Overall, the cited main message to motivate parents to vaccinate their daughters was for prevention of a disease (in general, regardless of vaccine type). However, in the case of HPV vaccination, this prevention message was specifically against cervical cancer. Television was consistently cited as the main source of information, followed by one-on-one-discussions, and information handed out at school. Pediatricians and OB/GYNs more frequently preferred messages focusing specifically on cervical cancer prevention than the other medical specialties surveyed.

The finding that mothers were the most influential in the decision to vaccinate girls is consistent with other studies conducted globally. A systematic review of 101 qualitative and quantitative studies analyzing the roles of family members in HPV vaccination uptake, showed that a parent, most often the mother, was responsible for making the ultimate decision about HPV vaccination. Interestingly, parent-adolescent decisions have been shown to often be concordant, yet providers were often sought for guidance in case of disagreement¹⁷. In a study surveying mothers and daughters separately across three pediatric clinical settings in the US, most interviewed mothers reported making the decisions regarding HPV vaccination, and daughters generally trusted this decision¹⁸. Two HPV vaccination studies from Rwanda and Vietnam showed that interpersonal communication between family members and government representatives led to increased HPV vaccination uptake^{19,20}. In Rwanda, parents were instrumental in achieving a 93% HPV vaccination coverage in a school-based campaign built on a strong public messaging addressing questions related to the vaccine's safety and efficacy¹⁹. In Vietnam, parents were also key in

HPV vaccination uptake due to the consistent involvement with clinical teams and local authorities in the vaccination process²⁰.

One important study finding is that providers' messages that tend to motivate parents to vaccinate their daughters against HPV were those emphasizing the key role of HPV vaccination in preventing cervical cancer. This agrees with an international study showing that knowledge regarding HPV, cervical cancer, and HPV vaccination among both providers and teenage girls was positively associated with HPV vaccination uptake in several geographical areas²¹. Thus, it is crucial that health professionals in low and middle-income countries emphasize the importance of HPV vaccination to prevent cervical cancer and other HPV-associated cancers when talking with parents and adolescent girls. Materials to educate healthcare practitioners, adolescents and their parents with adequate messages regarding HPV vaccination are needed to increase HPV vaccination uptake, especially in regions where uptake remains relatively low.

Further, HPV vaccination uptake rates among U.S. adolescents has differed by provider-type, with the highest rates among family physicians, pediatricians, and OB/GYNs^{22,2}. However, very few studies in U.S. and globally have analyzed the variation in HPV vaccination messaging among different types of providers²⁴. A novel finding from the present multi-site study is that pediatricians, midwives, and OB/GYNs were more likely to convey HPV vaccination messages specifically focused on cervical cancer prevention, as compared to family physicians and nurse practitioners who generally cited other prevention messages. Consistently, a study from Malaysia found that pediatricians and family physicians were more likely to emphasize the effectiveness of HPV vaccine for cervical cancer prevention, rather than for STI prevention²⁴. Thus, countries should consider promoting effective messages for HPV vaccination uptake that reach all clinical providers of teenage clients, including family physicians and nurse practitioners. Efforts are also

being made in several countries to increase vaccination education for adolescents in general, with referrals in collaboration with other types of providers who regularly serve adolescents patients (i.e. pediatric dentists²⁵, pharmacists²⁶).

Well-chosen communication messaging should optimally help educate parents about HPV vaccine safety, efficacy, and cost coverage/reimbursement. Healthcare providers cited that television was the best information delivery medium, followed by one-one-discussions with a healthcare provider, and information handed out at school. For instance, South Korea launched a national HPV vaccine program in June 2016 among 12-13 year- old girls. Our survey in Korea found that information obtained in school was a main source of information about HPV vaccination, likely attributable to South Korea's notably high education attainment rates²⁷. Two thirds of providers also highlighted the increasing influence of internet-based platforms including social media and websites. A study conducted among 889 caregivers in North Carolina similarly showed that health care providers (88%) and internet (65%) were the preferred sources for information about HPV vaccination, and that vaccination uptake was positively associated with increased awareness, knowledge, and media use²⁸. A qualitative study in the United Kingdom found that exposure to media and direct-to-consumer advertising on HPV vaccination prompted parents and their daughters to seek further information about HPV vaccination, most often through television commercials, but also magazines, news programs, radio, and internet²⁹.

There is a persistent debate concerning the best messages to promote HPV vaccination among studies conducted primarily in high-income countries: Two effective strategies have been found as good communication techniques: “gained-framed messages,” which emphasize the benefits of performing a desirable behavior (e.g., if you get vaccinated, you will reduce your chance of developing cervical cancer) versus “loss-framed messages,” which focus on the disadvantages of

not performing the advocated behavior (e.g., if you don't get vaccinated, you will increase the chance of developing cervical cancer)³⁰. A meta-analytic review suggested that parents might be persuaded more to vaccinate their children by loss-framed rather than gain-framed messages³¹. A Canadian study of 367 fathers and mothers investigating the effects of framed messages on parents' intentions to have their children vaccinated against HPV, showed that each parent processed messages differently depending on the child's sex. Parents who are the same sex as the child tended to be persuaded by loss-framed messages (perhaps due to more involvement in the child's sexual health), while parents who are the opposite sex to their child may be mostly persuaded by gained-framed messages. In their conclusion, the authors did not favor one approach over another, but rather preferred the mixed-framed messages featuring both positive and negative information about a health behavior³².

Among study strengths, our data on adolescent providers from different medical specialties across five geographically diverse regions provided important insights on HPV vaccination messages across and within countries. Attitudes and beliefs from these clinicians highlight the difficulties associated with HPV vaccination uptake in some countries where anti-HPV vaccination campaigns prevail, despite numerous reports demonstrating the safety and high tolerability of HPV vaccination³³. This underlines the importance of developing cultural-, religious- and ethnic-specific messages to enhance the uptake of HPV vaccination³⁴. For instance, one health provider mentioned that parents are often inundated by religious concerns and negative messages about HPV vaccination, making it more difficult to convince them to vaccinate their child against HPV. Another family physician cited a potential religious concern in Malaysia, noting that the ingredients in the HPV vaccine are halal (i.e., lawful in traditional Islamic law).

Among study limitations, the convenience sampling achieved from a relatively small size of providers across two high income and three upper-middle income countries may lead to a selection bias with non-generalizability of study findings. Secondly, surveyed providers reported only on girls' vaccination, rather than on girls and boys, given that most current national HPV vaccination programs in low and middle-income countries do not currently include coverage of HPV vaccination for boys in their immunization programs. However, global gender-neutral vaccination policies include the promotion of HPV vaccination in adolescent boys as well.

Overall, providers cited a prevention message against cervical cancer as optimal to motivate parents to vaccinate their daughters against HPV. Television was consistently cited as the main source of information on HPV vaccination, followed by one-on-one-discussions. Pediatricians and OB/GYNs more often preferred messages focusing specifically on cervical cancer prevention than the other medical specialties surveyed.

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. International Agency for Research on Cancer; 2013. Available at: <http://globocan.iarc.fr>. Accessed May 24, 2015.
2. Walboomers JM, Jacobs MV, Manos MM, et al. HPV is a necessary cause of invasive cervical cancer worldwide. *J Pathol* 1999;189: 12-19.
3. Ginsburg O, Bray F, Coleman MP, et al. The global burden of women's cancers: a grand challenge in global health. *Lancet* 2017; 389: 847-860.
4. Doorbar J, Egawa N, Griffin H, et al. Human papillomavirus molecular biology and disease association. *Rev Med Virol* 2015; 25: 2-23.

5. Garland SM, Smith JS. Human papillomavirus vaccines: current status and future prospects. *Drugs* 2010; 70:1079-98.
6. Zhai L, Tumban E. Gardasil-9: A global survey of projected efficacy. *Antiviral Res* 2016 ;130:101-109.
7. World Health Organization. Immunization, Vaccines and Biologicals. Available at <http://www.who.int/immunization/diseases/hpv/en>. Accessed February 15, 2017.
8. Bruni L, Diaz M, Barrionuevo-RL, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. *Lancet Glob Health* 2016; 4: e453–463.
9. Sherris J, Friedman A, Wittet S, et al. Chapter 25: Education training, and communication for HPV vaccines. *Vaccine* 2006; 24:210-218.
10. Gilkey MB, Calo WA, Moss JL, et al. Provider communication and HPV vaccination: The impact of recommendation quality. *Vaccine* 2016; 34: 1187-1192.
11. Walling EB, Benzoni N, Dornfeld J, et al. Interventions to Improve HPV Vaccine Uptake: A Systematic Review. *Pediatrics* 2016;138:1-13.
12. Gonik B. Strategies for fostering HPV vaccine acceptance. *Infect Dis Obstet Gynecol* 2006; 36797: 1-4.
13. Bingham A, Drake JK, LaMontagne DS. Sociocultural Issues in the Introduction of HPV vaccine in Low-Resource Settings. *Arch Pediatr Adolesc Med* 2009;163: 455-461.
14. Larson HJ, Wilson R, Hanley S, et al. Tracking the global spread of vaccine sentiments: the global response to Japan's suspension of its HPV vaccine recommendation. *Hum vaccine Immunother* 2014;10: 2543-2550.

15. R Studio [computer program]. Version 3.5.0. Vienna, Austria: R Core Team; 2018.
16. Kim HY. Statistical notes for clinical researchers: Chi-squared test and Fisher's exact test. *Restor Dent Endod* 2017; 42:152–155.
17. Gilkey MB, McRee AL. Provider Communication about HPV vaccination: A systematic review. *Hum Vaccin Immunother* 2016;12:1454–1468.
18. Griffioen AM, Glynn S, Mullins TK, et al. Perspectives on decision making about HPV vaccination among 11- to 12-year old girls and their mothers. *Clinical Pediatr (Phila)* 2012; 51:560-568.
19. Binagwaho A, Wagner CM, Gatera M, et al. Achieving high coverage in Rwanda's national HPV vaccination programme. *Bulletin of the World Health Organization* 2012; 90: 623-628.
20. Cover JK, Nghi NQ, LaMontagne DS, et al. Acceptance patterns and decision-making for HPV vaccination among parents in Vietnam: An in depth qualitative study post-vaccination. *BMC Public Health* 2012; 12: 1-14.
21. Hopkins TG, Wood N. Female Human Papillomavirus vaccination: Global uptake and the impact attitudes. *Vaccine* 2013; 31:1673-1679.
22. Leddy MA, Anderson BL, Gall S, et al. Obstetrician-gynecologists and the HPV vaccine: practice patterns, beliefs, and knowledge. *J Pediatr Adolesc Gynecol* 2009; 22 (4): 239-246.
23. Vadaparampil ST, Kahn JA, Salmon D, et al. Missed clinical opportunities: Provider recommendations for HPV vaccination for 11-12 year old girls are limited. *Vaccine* 2011;29:8634-8641
24. Wong LP. Physicians' experiences with HPV vaccine delivery: Evidence from developing country with multiethnic populations. *Vaccine* 2009; 27:1622-1627.

25. Hosking YP, Cappelli D, Donly K, et al. HPV Vaccination and the role of the Pediatric Dentist: Survey of Graduate Program Directors. *Pediatr Dent* 2017; 39: 383-389.
26. Hastings TJ, Hohmann LA, McFarland SJ, et al. Pharmacists' Attitudes and Perceived Barriers to Human Papillomavirus (HPV) Vaccination Services. *Pharmacy (Basel)* 2017; 5:1-14.
27. Education Policy Outlook Korea. OECD Better Policies for Better Lives. Available at: <http://www.oecd.org/education/Education-Policy-Outlook-Korea.pdf>. Accessed November 2016.
28. Hughes J, Cates JR, Liddon N, et al. Disparities in how parents are learning about the HPV vaccine. *Cancer Epidemiol Biomarkers Prev* 2009;18 :363-372.
29. Manika D, Ball JG, Stout PA. Factors associated with the persuasiveness of direct-to-consumer advertising on HPV vaccination among young women. *J Health Commun* 2014;19: 1232-1247.
30. Gerend MA, Shepherd JE. Using message framing to promote acceptance of the human papillomavirus vaccine. *Health Psychol* 2007; 26:745-752.
31. O'Keefe DJ, Nan X. The relative persuasiveness of gain- and loss-framed messages for promoting vaccination: a meta-analytic review. *Health Commun* 2012; 27:776-783.
32. Gainforth HL, Cao W, Latimer-Cheung AE. Message framing and parents' intentions to have their children vaccinated against HPV. *Public Health Nurs* 2012; 29: 542-552.
33. Stillo M, Santistev PC, Lopalco PL. Safety of HPV vaccines: a review. *Expert Opin Drug Saf* 2015; 14 : 697-712.
34. Lechuga J, Swain GR, Weinhardt LS. Impact of framing on intentions to vaccinate daughters against HPV: A Cross-Cultural Perspective. *Ann Behav Med* 2011; 42:221–226.