Published in final edited form as:

Cancer Causes Control. 2018 November ; 29(11): 1115–1130. doi:10.1007/s10552-018-1085-1.

Acceptability of Two-Versus Three-Dose Human Papillomavirus Vaccination Schedule among Providers and Mothers of Adolescent Girls: A Mixed-Methods Study in Five Countries

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Abstract

Purpose: The World Health Organization revised its HPV vaccination recommendations to include a two (2-) dose schedule for girls aged 15 years. We investigated acceptability of 2-versus 3-dose schedule among adolescent vaccination providers and mothers of adolescent girls in five countries.

Methods: Adolescent vaccination providers (N=151) and mothers of adolescent girls aged 9-14 years (N=118) were recruited from Argentina, Malaysia, South Africa, South Korea, and Spain. We assessed providers' preference for a 2-versus 3-dose HPV vaccination schedule via quantitative

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Conflict of interest

The remaining authors have no conflicts of interest to disclose.

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surveys. Mothers' attitudes toward a 2-dose schedule were assessed through focus group discussions.

Results: Most adolescent providers preferred a 2-over 3-dose HPV vaccination schedule (overall: 74%), with preference ranging from 45.2% (South Africa) to 90.0% (South Korea). Lower cost, fewer clinic visits, and higher series completion were commonly-cited reasons for 2-dose preference among providers and mothers. Safety and efficacy concerns were commonly-cited barriers to accepting a 2-dose HPV vaccination schedule among providers and mothers. Mothers generally accepted the reduced schedule, however, requested further information from a trusted source.

Conclusions: Adolescent vaccination providers and mothers preferred the 2-dose over 3-dose HPV vaccination schedule. Acceptability of a 2-dose HPV vaccination could be improved with additional information to providers and mothers on HPV vaccination safety and efficacy.

Keywords

vaccination; acceptability; human papillomavirus; dose; adolescent; providers; parents; focus-groups

INTRODUCTION

Globally, human papillomavirus (HPV) is the most common sexually transmitted infection and has been established as the cause of cancers of the cervix, anus, vagina, vulva, penis, and oropharynx[1]. Highly effective prophylactic vaccines have been developed to prevent HPV persistence and HPV-associated cancers in women and men. Since 2006, HPV vaccination has been introduced globally into national immunization programs for girls in 71 countries, and for boys in 11 countries[2]. Countries with national immunization programs have seen varied national coverage of HPV vaccination due to programmatic barriers including cost, lack of knowledge of HPV and cervical cancer, vaccination safety concerns, and dose completion difficulties for patients and providers [3–6]. Programmatic barriers of HPV vaccination uptake are of particular concern in low- and middle-income countries (LMICs), with the greatest global burden of HPV-related cancers, particularly cervical cancer[7].

Offering an HPV vaccination schedule with fewer doses is one promising approach to reduce barriers to vaccination. Clinical trials have demonstrated that a 2-dose schedule elicits and sustains non-inferior immune responses in adolescent girls aged <15 years old as compared with the 3-dose regimen, over a five-year time period [8–12]. In 2014, the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) revised its HPV vaccination recommendation in accordance with emerging scientific evidence, and now globally recommends adolescents under 15 years of age receive a 2-dose schedule, with 3-doses still recommended for adolescents 15 years and older and the immunocompromised or infected with human immunodeficiency virus (HIV)[13]. Transitioning to a 2-dose schedule has the potential to increase HPV vaccination coverage at a reduced cost if efforts are focused on vaccinating the WHO recommended target group. Availability of a 2-dose

schedule presents an important opportunity to substantially reduce programmatic barriers to providing HPV vaccination.

Mothers are usually the primary health care decision maker for their children[14]. A mother's HPV vaccination intention for her adolescent child is influenced by several factors including her attitudes towards HPV vaccination, perceptions of community opinion regarding HPV vaccination, and perceived difficulty of getting HPV vaccination[15]. These intentions are further influenced by health care providers. High quality provider recommendation is the primary influencer of HPV vaccination initiation among mothers for their adolescents and is positively correlated with higher rates of HPV vaccination in adolescent girls [16–19].

Previous studies have evaluated HPV vaccination acceptability in parents of eligible adolescents and health care providers [5,20–23]. However, to our knowledge, no research study has assessed provider and maternal perceptions of a 2-versus 3-dose HPV vaccination schedule across countries using a standardized questionnaire. Further data are needed on providers' and mothers' acceptance of a lower dose HPV vaccination schedule to inform the global implementation of HPV vaccination programs for adolescents, particularly as prior studies have identified knowledge of HPV vaccination efficacy and safety as a major barrier to three-dose HPV vaccination uptake among adolescents [24].

Our primary aim was to solicit provider and mother opinions of the acceptance of a 2-dose HPV vaccination schedule in five countries, including Argentina, Malaysia, South Africa, South Korea, and Spain. We included distinct geographical continents to inform global implementation of 2-dose HPV vaccination and invited international investigators globally known to the HPV field. Selected countries included a variety of contexts for HPV vaccination availability. Argentina, Malaysia, and Spain expanded their respective National Immunization Programs to cover the cost of HPV vaccination for female adolescents in 2011, 2010, and 2007 respectively, prior to this study. However, South Africa and South Korea did not have a national program covering the cost of HPV vaccination at the time this survey was completed. Here, we present data on the acceptability of a 2-versus 3-dose HPV vaccination schedule among both adolescent health care providers and mothers of adolescent girls. Data from in-country providers contributes new insights into HPV vaccination acceptability in countries with little or no existing research on provider perceptions of the updated 2-dose schedule of HPV vaccination.

METHODS

Study Participants

Providers(Quantitative): We implemented a cross-sectional survey of health care providers who administer vaccination to adolescents, hereafter referred to as adolescent vaccination providers. The survey was conducted in five countries from diverse geographical and sociocultural regions, including Argentina, Malaysia, South Africa, South Korea, from October 2013 to April 2014. Study staff identified eligible providers with the authority to administer adolescent vaccines by examining each country's medical regulations. Further site-specific details on recruitment of providers are available in Appendix 1. Providers were

eligible to participate if they actively administered adolescent vaccines. Adolescent vaccination providers were identified via non-probability convenience sampling and recruited through mail, email, phone, or in-person. Participating providers were compensated for their time and associated travel required for the study interview.

Mothers (Qualitative): Four focus group discussions were conducted in each country between November 2013 and April 2014, including at least one focus group with mothers of vaccinated daughters and at least one focus group with mothers of unvaccinated daughters, except Spain where six mothers of unvaccinated daughters completed individual semi-structured interviews rather than focus group discussions. Given high HPV vaccination coverage in Spain, local investigators were unable to efficiently recruit enough participants who had not vaccinated their daughters to participate in focus group discussion format. To address this concern, the Spain study site conducted 6 individual interviews with women who had not vaccinated their daughters. Mothers were recruited using non-probability convenience sampling from medical offices, health centers, or schools (Appendix 1). To be eligible, mothers had to have a daughter old enough to receive HPV vaccination, based on each country's vaccination guidelines at the time of data collection up to 14 years of age (age: 9 years in South Africa; 11 years in Argentina/South Korea/Spain; 13 years in Malaysia). Eligible, interested mothers were stratified into focus groups based on whether their daughter was either (i). vaccinated or (ii). unvaccinated. A total of 124 mothers (70 with vaccinated daughters, 54 with unvaccinated daughters) were enrolled across the five countries (Argentina [n = 23]; Malaysia [n = 26]; South Africa [n = 21]; South Korea [n = 31]; and Spain [n = 23]), with a median of 5.5 participants per focus group.

Study collaborators in each country secured Institutional Review Board (IRB) approval from their respective institutions prior to data collection. UNC study staff received IRB approval for analysis of de-identified secondary data.

Measures

Providers (Quantitative): Surveys were administered in-person or by phone to providers. A trained study interviewer collected information on providers' demographic information and experiences administering HPV vaccination to adolescent girls within the age guidelines for each country. Providers were given different questionnaires based on whether they had previously administered HPV vaccination. A total of eight questions assessed attitudes towards willingness for initiation and for completion of a 2-versus 3-dose HPV vaccination schedule, as well as anticipated successes and barriers to a 2-dose schedule (see Appendix 2). The response to the following question was used as primary measure of preference for the 2-dose HPV vaccination, i.e. the outcome for multivariable regression analyses: "If a 2-dose HPV vaccine were to become available, which would you recommend more frequently: A 3-dose HPV vaccine or a 2-dose HPV vaccine?" Country study staff entered de-identified data into English language EpiData forms, translating data into English when necessary.

Mothers (Qualitative): Each focus group discussion followed a semi-structured script that assessed mothers' attitudes towards various aspects of adolescent HPV vaccination, including questions to evaluate knowledge of cervical cancer, willingness to obtain the HPV

vaccination for their daughters, barriers and facilitators to obtaining the HPV vaccination for their daughters, and efficacy of a 2-dose schedule. The present analysis pertains to focus group discussions around maternal attitudes towards a 2-dose compared to 3-dose HPV vaccination schedule. Focus group moderators asked questions from a discussion guide, and additional questions emerged through probing and clarifying statements (see Appendix 3).

Analysis

Providers (Quantitative)—Data obtained from providers were double-entered in English by staff in each country as a measure for quality control of data. Identified discrepancies were resolved in consultation with each site's primary investigator. A final de-identified data set was sent to UNC for final data cleaning and analysis. Univariate analyses were conducted across country sites to assess baseline characteristics of providers and mothers of adolescents, and to evaluate adolescent vaccine practices and attitudes among providers. Multivariable logistic regression was utilized to identify predictors of 2-versus 3-dose preference for HPV vaccination. Models were fit to estimate multivariable-adjusted odds ratios (aORs) and associated 95% confidence intervals (CIs) for the following predictor variables separately, adjusted for country of origin: type of provider; providers' years of practice; whether provider administered HPV vaccination; provider's average number of adolescent female patients seen per month; providers' perceptions of efficacy of 2-dose HPV vaccination; and provider's perceptions of potential side effects of the 2-dose as compared to 3-dose HPV vaccination. All quantitative analyses were conducted in SAS 9.3 (SAS Institute Inc., Cary, NC).

Mothers (Qualitative)—In-country researchers facilitated the verbatim transcription of focus group discussion recordings and their translation into English. Translations were reviewed by in-country study staff who were native speakers of the language used during the focus group discussion 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.

An experienced qualitative researcher (McDonald) supervised data management and analysis, which includes the following procedures. Cleaned transcripts were entered into ATLAS.ti (ver. 7, Berlin, Germany) for thematic analysis[25,26]. We began by using a structured codebook based on the study aim and the focus group discussion script. A thematic analysis framework was used to code the data. Additional codes were added as they emerged from the data through an iterative process: one focus group discussion transcript from each country was then reviewed independently by two research assistants and coded, along with additional emergent themes. Next, these transcripts were compared and inconsistent coding decisions were discussed until a final agreement was reached. Additional emergent codes were incorporated into the codebook, and remaining transcripts were coded and reconciled using the same procedure [27–30]. Below, qualitative data are summarized thematically.

RESULTS

Providers (Quantitative Analysis)

Providers' Medical Practice—Of 353 providers contacted, 151 were enrolled across the five countries (Argentina [n=30]; Malaysia [n=30]; South Africa [n=31]; South Korea [n=30]; and Spain [n=30]). The most common practitioner types were family, internal, or general practitioners (31%); obstetrics/gynecologists (OB/GYN) (26%); and pediatricians (22%) (Table 1). All adolescent providers from Argentina (100%), and most from Spain (87%) and Malaysia (77%) had provided HPV vaccination to adolescents, compared with half in South Korea (50%) and about one-third in South Africa (36%) (Table 2).

Providers' Attitudes towards a 2-Versus 3-dose HPV Vaccination Schedule—Most providers (75%) reported that they would recommend a 2-dose compared to 3-dose schedule, ranging from 45 in South Africa to 90% in South Korea (Figure 1). Most common reasons for recommending a 2-dose vaccine more frequently to parents of adolescent girls were lower cost (Argentina: 27%; Malaysia: 53%; South Africa: 16%; South Korea: 60%; Spain: 47%), fewer office visits (10%, 30%, 19%, 67%, 70% respectively), higher series completion (67%, 3%, 19%, 50%, 63% respectively), and less pain (37%, 10%, 10%, 33%, 53% respectively) (Figure 2).

About one-third of providers noted that cost was the main barrier to HPV vaccination that a 2-dose schedule could address, ranging from 10% in Spain to 57% in Malaysia (Table 2). Fewer clinic appointments were cited as a main advantage of a 2-dose HPV vaccination schedule, ranging from 23% in Malaysia to 83% in Spain. When asked specifically about potential concerns of a 2-dose HPV vaccination schedule, providers cited concerns regarding the possibility of lower vaccine efficacy (54%), ranging from 10% of providers in South Africa to 77% in South Korea. Several providers stated they would need more information on the efficacy of the 2-dose HPV vaccination (61%), ranging from 19% of providers in South Africa to 87% in South Korea.

Fewer than half of providers from South Africa preferred the 2-dose HPV vaccination (45%). Additionally, we observed an increase in the proportion of 2-dose preference of HPV vaccination among providers with 20 female adolescent patients or more (79%), as compared to providers with <20 per month (70%) (Table 3). Adolescent vaccination providers were more likely to prefer the 2-dose than the 3-dose HPV vaccination schedule if they believed that 2-dose HPV vaccination is as effective as a 3-dose vaccination schedule (adjusted OR: 8.25, 95% CI: 3.09-22.03) (Table 3). Provider preference for a 2-versus 3-dose vaccination schedule did not appear to be associated with any other factor examined, including type of provider, provider years of practice, HPV vaccination provision status, average number of adolescent girls seen in provider's clinic per month, and provider's opinion of whether the 2-dose HPV vaccination schedule would have more side effects than 3-dose vaccination.

Mothers of adolescent daughters (Qualitative Analysis)

Qualitative data provided insight into mothers' rationale regarding their preferences for the 2-versus 3-dose HPV vaccination. The focus group discussions revealed a diversity of mothers' understanding of the basics of vaccination and the immunization process, the HPV virus, and the etiology of cervical cancer across the five countries and within focus groups (data not shown). Table 4 describes emergent themes that, while seen to some degree in all groups, were salient to each country group. Focus group discussions with mothers of unvaccinated girls voiced similar perceived advantages and concerns to those of vaccinated girls, with slight exceptions. Many themes related to the 2-versus 3-dose HPV vaccination were consistent across focus groups.

Perceived Advantages of a 2-Versus 3-dose HPV Vaccination Schedule

Convenience: Most women recognized that a 2-dose HPV vaccination schedule would be easier to complete, and would be more convenient and timesaving compared to a 3-dose schedule.

"I think that two doses, because of some mothers that sometimes don't take them [daughters], they already have a hard time taking them to the outpatient clinic. ... It would be easier for them." – Argentina Vaccinated Focus Group

"Just as if they want to make a one-dose vaccine, even better, you think, if it covers just the same and you only have to get shot once, great!" – Spain, Vaccinated Focus Group

However, other mothers said that the convenience afforded by the 2-dose was only acceptable if they were sure it provided "protection" as strong as that of the 3-dose HPV vaccination.

"Then twice is way better. Under the assumption that they have same efficacy, twice is more convenient." – Korea, Unvaccinated Focus Group

Favorable attitude towards scientific innovation: Many mothers across countries rationalized that the change in dosing schedule is based on new research and scientific innovation. These mothers positively associated scientific innovation with the updated 2-dose vaccination schedule.

"That increases my reliability [how reliable she thinks the vaccine is] since it seems like the improved version, like Samsung introducing newer version – South Korea, Unvaccinated Focus Group

"There must be a reason. If the reason is good, then we have to accept it. Because the research has been done. If the evidence states that 2 is sufficient we have to follow." – Malaysia, Vaccinated Focus Group

Perceived Barriers to a 2-Versus 3-dose Schedule

Concerns about the strength of vaccination: Across country sites, concerns surfaced regarding the efficacy of the HPV vaccination if it were reduced from three to two doses. Some mothers assumed that the 2-dose schedule would include the same amount of drug as

the 3-dose schedule in fewer injections, which increased concerns about side effects, both short term and long term.

“Okay, because maybe then the dose is much larger and there might be more side effects and such, right? Like, we also have to take that into account. Putting three doses in one.” – Spain, Vaccinated Focus Group

“No. In my case, I would ask the pediatrician about two or three times, really. Because if it is three doses, and then it’s only two, they would be stronger, 11 years old and such a strong vaccination, I don’t think so.” – Argentina, Vaccinated Focus Group

Cost: Like providers, cost was an important consideration for mothers’ decision making.

“Before I have to get the full information as to why is the different between the 3-doses and the 2-doses before I can; and I have to know why they are different and why the other one is cheaper and why the other one is expensive before I will be able to say to other people which one to take.” – South Africa, Unvaccinated Focus Group

Participating countries had different national health care payment systems, and socioeconomic status varied considerably across participants, making it difficult to compare responses regarding cost among focus groups. For example, in Argentina, HPV vaccination is part of the mandatory vaccination policy for adolescents and is free of cost. Mothers in South Korea and South Africa attributed new recommendations with effectiveness, noting that even if the 2-dose was more expensive, they would still choose it.

“I will have it [the two dose] if it’s much better than the previous one even though it’s more expensive...” – South Korea, Unvaccinated

“When it comes to prevention the cost comes last, cost should not be an issue. As long as you are preventing, cost should not be an issue.” – South Africa, Vaccinated Focus Group

Information Needed to Accept a 2-dose Vaccination Schedule

Desire for reliable information from trusted sources: Mothers from both focus group discussion groups (with vaccinated and unvaccinated daughters) expressed interest in receiving individualized, concise information from a trusted provider. Mothers generally respected the opinions of doctors and researchers, however, they expressed interest in receiving consistent, reliable information first-hand.

“...the truth is that we are not thoroughly informed because there was no campaign. There is a campaign to vaccinate, but not one to inform...” – Argentina, Vaccinated Focus Group

Most women wanted to make sure they had all information to make the right decision. Interestingly, after hearing about the 2-dose HPV vaccination, some mothers of vaccinated daughters questioned their decision to vaccinate their daughter with the 3-dose schedule.

“When they make the change, they don’t tell you why. Then we don’t know whether it is better or if what we did was wrong, if it is better now.” – Argentina Vaccinated Focus Group

Many mothers did not understand what HPV vaccination protected against, or the associated side effects, which coincided with lower knowledge about HPV vaccination and cervical cancer. All focus group discussions included varying degrees of knowledge of the efficacy and potential side effects of HPV vaccination.

“If the effect is the same, then, I don’t know, I don’t know how vaccines work or don’t.” – Spain, Vaccinated Focus Group

Discussion

In this mixed-methods study of five countries, adolescent health care providers and mothers of adolescent girls tended to prefer a 2-dose over a 3-dose HPV vaccination schedule. Providers cited that the 2-dose schedule addressed many barriers of the 3-dose schedule, with the potential for lower cost, fewer clinic visits, higher series completion, and less patient pain. Mothers generally preferred a reduced HPV vaccination schedule, citing greater convenience and favorable attitudes towards scientific innovation. Both providers and mothers, however, expressed some concerns and the need for more information regarding the relative safety and efficacy of 2-dose compared to 3-dose HPV vaccination. Our study findings are consistent with previous research suggesting that a 2-dose regimen can effectively address barriers to 3-dose HPV vaccination[31,32], including cost of HPV vaccination. Two-dose HPV vaccination has been shown to be more cost-effective when compared to 3-dose HPV vaccination in both the short- and long-term .

Provider recommendation is the primary predictor of HPV vaccination uptake[33]. The positive association between awareness of HPV vaccination, and HPV vaccination initiation and completion among parents of adolescents has been shown to depend on strong provider recommendation[34,35]. Providers across countries in our study had varying degrees of understanding of whether the efficacy and safety of a 2-dose HPV vaccination schedule was comparable to a 3-dose schedule. Previous studies have found that providers do not regularly recommend HPV vaccination for a several reasons, including ambiguity regarding who and what age group needs to receive the vaccine, and confidence in addressing parental concerns[36,37]. In our study, while providers generally supported a 2-dose HPV vaccination schedule, they had concerns regarding its efficacy and safety, and requested further information on these topics to feel more comfortable for their patient recommendations.

Like providers, mothers were generally accepting of a 2-dose HPV vaccination due to greater convenience and reduced cost. However, several mothers requested more information regarding efficacy and safety before making a confident decision. Our focus group findings echo previous research regarding mothers’ attitudes towards a 3-dose schedule. Qualitative research conducted among women in South Africa and Ohio Appalachia highlighted the importance of mother and female caretakers in health decision making for the initiation of the 3-dose HPV vaccination for their daughters; support for HPV vaccination was observed,

with concurrent concerns related to the vaccination's cost and side effects[14]. This simultaneous support and concern of HPV vaccination is reflected in other studies in LMICs related to the 3-dose schedule [38–42]. In the current study, concerns related to cost had the potential to be addressed by a 2-dose schedule, although concerns related to resulting changes in vaccine efficacy and associated side effects remained to varying degrees by country.

Notable variability in knowledge of both providers and parents has been identified in a global systematic review that described WHO's SAGE definitions of vaccination hesitancy as influenced by several factors including confidence, complacency, and convenience[43]. This SAGE review noted that factors related to vaccination hesitancy varied widely by country, and were further nuanced by social and cultural norms [43]. A systematic review of Sub-Saharan Africa similarly showed high levels of willingness and acceptability of the 3-dose HPV vaccination among adolescent girls, parents of adolescents, and health care workers while identifying notable gaps in knowledge and education regarding HPV, HPV vaccination, and cervical cancer among these same groups.

Study advantages included the use of a standardized mixed methods design across five geographically diverse sites, which allowed for better understanding of similarities and differences in acceptability of 2-dose HPV vaccination schedule across countries. While many LMICs have made successful transitions from a 3-to 2-dose HPV vaccination schedule, social mobilization and acceptability remain important communication strategies to promote uptake, particularly through face-to-face interactions[44]. Since HPV vaccination perceptions and knowledge differed by country, messaging and educational campaigns for a 2-dose vaccination schedule will need to be tailored to the specific social, economic, and political climate of the region of introduction. This approach is supported by previous research investigating various means of achieving high HPV vaccination coverage in LMICs[5], as well as studies conducted in high-income countries that recognize the need for multiple strategies for vulnerable population sub-groups.

Limitations of this study included a relatively small provider sample size and non-probability based sampling strategy of providers, limiting the generalizability of the findings within these countries. Small sample sizes of providers and mothers precluded the use of statistical tests to assess group differences between countries, or between mothers of vaccinated and unvaccinated daughters. Additionally, due to small sample size, we were unable to account for clustering by country in our quantitative analysis. With larger sample sizes by country, we may have observed significant odds ratios within logistic regression analyses. Given that we utilized convenience sampling to recruit mothers of adolescents, mothers who participated in focus group discussions were more often from urban areas, and thus likely with greater access to medical providers and health clinics. In our study, we did not directly interview adolescents regarding their opinions of HPV vaccination as mothers are usually the primary health care decision makers for their children and due to issues regarding consent for adolescent participants. Finally, given that the focus group guide was based on prior literature of barriers to HPV vaccination, we acknowledge that this approach was more pragmatic than a ground-up, inductive approach to elicit participants' potential concerns about HPV vaccination.

Our findings indicate that both providers and parents could benefit from focused education regarding a 2-dose HPV vaccination schedule. While some logistical barriers to HPV vaccination acceptance are addressed by a reduced 2-dose vaccination schedule, concerns related to potential for increased side effects and lower efficacy seem to remain, despite general acceptability of HPV vaccination. Though mothers' acceptability of a 2-dose HPV vaccination schedule varied by country site, this acceptability could be enhanced by additional information regarding safety and efficacy by providers. These findings underscore the importance of a strong health provider recommendation for a 2-dose HPV vaccination to bolster mothers' acceptance of the vaccination for their daughters, including opportunities to address any concerns related to side effects and efficacy. A strong recommendation with patient education from a trusted healthcare provider has been shown to be a primary vaccination mediator among parents of adolescents [16–19]. Evidence from the current study supports this finding for a 2-dose HPV vaccination schedule. Providers generally accepted a 2-dose schedule, although but it is unknown how strong their recommendations would be as knowledge about safety and efficacy varied across sites.

Future implementation science research should be focused on equipping providers with the knowledge and optimal communication skills to improve HPV vaccination discussions with parents from varying socioeconomic and education levels. Literature from high-income countries has suggested that HPV vaccination availability and promotion alone is not enough to influence significant uptake, and identified the need for comprehensive approaches that target multiple levels of the socioecological model [45–47] in culturally responsive ways[14].

Reducing the HPV vaccination dosing schedule from 3-to 2-doses has the potential to reduce logistical barriers for patients and providers. This, combined with increased access and culturally relevant communication campaigns that promote high-quality recommendations from providers can effectively increase vaccination rates in LMICs and reduce the burden of HPV-related cancers for future generations. Knowledge generated from this study can inform future programmatic decisions as more countries adopt a 2-dose vaccination schedule, and potentially a 1-dose schedule for HPV vaccination, if recommended based on currently evolving scientific evidence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors gratefully acknowledge the participants of this study. The authors thank Suzanne Landi, Shoshana Goldberg, and Sara Smith for their assistance in developing this manuscript. JYI was supported by a NIH NRSA individual predoctoral fellowship (F31-CA210474-01A1).

Funding

This study was funded by GlaxoSmithKline Biologicals SA (Study ID: 117339); all data collection, analysis and interpretation was conducted by study co-authors, and GSK had the opportunity to review this paper. GSK did not have input into the research data collection, analysis, or interpretation of results.

Jennifer S. Smith has received research grants, served on paid advisory boards, and/or been a paid speaker for GSK group of companies and Merck & Co., Inc. over the past five years.

Abbreviations

HIV	human immunodeficiency virus
HPV	human papilloma virus
LMIC	low and middle income country
SAGE	Strategic Advisory Group of Experts
STI	sexually transmitted infections
WHO	World Health Organization

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Figure 1:

If a 2-dose HPV vaccine were to become available, which would you recommend more frequently: A 3-dose HPV vaccine or a 2-dose HPV vaccine?

Figure 2:

[If 2-dose] Why would you recommend the 2-dose HPV vaccine more frequently to parents of girls?*

*Response may not add up to 100%; Multiple responses possible.

Table 1.

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

Quantitative Survey of Adolescent Providers (n = 151)						
	Argentina (n = 30)	Malaysia (n = 30)	South Africa (n = 31)	South Korea (n = 30)	Spain (n = 30)	Overall (n = 151)
Type of provider [*]						
Family/internal medicine, general practice	17%	87%	26%	20%	7%	31%
OB/GYN	40%	7%	23%	40%	20%	26%
Pediatrician	43%	3%	--	40%	23%	22%
Nurse/nurse practitioner	--	10%	32%	--	13%	11%
Midwife	--	--	7%	--	23%	6%
Place of vaccine provision [†]						
Clinic	83%	93%	52%	9%	80%	80%
Hospital	40%	3%	48%	7%	27%	25%
School	--	3%	16%	--	10%	6%
Type of vaccine provision						
Private only	37%	93%	36%	100%	3%	54%
Public only	13%	--	55%	--	73%	29%
Both	50%	3%	10%	--	23%	17%
Provider catchment area	San Luis Province Olivos and Vicente López City of Rosario City of San Lorenzo City of San Genaro City of Buenos Aires	Putrajaya Selangor state Kuala Lumpur	Pretoria Mamelodi Atteridgeville	Seoul Incheon Bundang, Bucheon Ilsan	Hospitalet de Llobregat Granollers Sabadell Llavaneres Esplugues de Llobregat Cerdanyola Reus Gerona Puigcerdà La Poble de Segur	
Focus Group Discussions of Mothers of Adolescent Girls (n = 118)						
	Argentina (n = 23)	Malaysia (n = 26)	South Africa (n = 21)	South Korea (n = 31)	Spain (n = 23)	Overall (n = 118)

Quantitative Survey of Adolescent Providers (n = 151)					
Location of FGD	Argentina (n = 30)	Malaysia (n = 30)	South Africa (n = 31)	South Korea (n = 30)	Spain (n = 30)
FGD 1	Buenos Aires	Kuala Lumpur	Atteridgeville	Seoul	Barcelona
FGD 2	San Isidro	Kuala Lumpur	Kwaggastrand	Seoul	Sabadell
FGD 3	San Isidro	Johor Bahru	Prinshof	Seoul	Montcada
FGD 4	Vicente López	Selangor	Kwaggastrand	Seoul	Mataró
Daughters vaccinated against HPV	74%	81%	33%	26%	74%
Daughters unvaccinated against HPV	26%	19%	67%	74%	26% [‡]
Mother's Age					
25-34 years	17%	0%	24%	0%	5%
35-44 years	42%	52%	52%	90%	64%
45+ years	42%	48%	24%	10%	32%
Educational Level					
Primary or less	54%	0%	4%	0%	18%
Secondary	29%	0%	44%	52%	50%
Higher than secondary	17%	100%	52%	48%	32%

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

* Provider types with < 3% of overall response were omitted from the Table 1 and included Pharmacists, Preventive Physicians, and Other

[‡] Places of vaccine provision with < 3% of overall response were omitted from Table 1 and included Other

[§] In Spain, mothers of unvaccinated daughters participated in in-depth interviews rather than FGDs

Location Description: ¹Buenos Aires Province, ²Santa Fe Province, ³Wilayah, ⁴township outside of Pretoria, ⁶Barcelona Province, ⁷Tarragona Province, ⁸Gerona Province, ⁹Lérida Province, ¹⁰Suburb of Pretoria

Table 2.

Adolescent vaccine practices and attitudes among providers in five countries (n = 151)

Country	Argentina (n=30)	Malaysia (n=30)	South Africa (n=31)	South Korea (n=30)	Spain (n=30)	Total (n=151)
Ever provided HPV vaccination to adolescents 9-14 years	100%	77%	36%	50%	87%	70%
Which do you think patients would follow more: a vaccine schedule of 0, 1 to 2 and 6 months, or a new schedule of 0 and 6 months? ^{*, †}						
0 and 6 months	60%	31%	61%	73%	67%	59%
0 and 2 months	--	41%	--	--	--	8%
0 and 1 months	10%	7%	--	--	--	3%
0, 1 to 2 and 6 months	13%	0%	3%	10%	3%	6%
No difference/the same compliance	10%	4%	29%	17%	20%	16%
Refused/Don't know	3%	7%	7%	--	3%	4%
Other [‡]	3%	10%	--	--	7%	4%
Do you think a 2-dose HPV vaccine would be as effective, more effective, or less effective compared to the 3-dose HPV vaccine? [*]						
As effective	43%	62%	26%	47%	45%	44%
Don't know/Not sure/Refused	43%	23%	16%	33%	48%	33%
Less effective	3%	7%	29%	13%	7%	12%
More effective	10%	7%	29%	7%	--	11%
Do you think it [HPV vaccination] would have more or fewer side effects than the 3-dose HPV vaccine? [†]						
The same	40%	79%	29%	37%	40%	45%
Fewer	50%	7%	48%	53%	31%	38%
Don't know/Not sure/Refused	10%	10%	19%	10%	28%	15%
More	0%	4%	3%	0%	0%	1%
Which obstacles [or barriers] would a 2-dose HPV vaccine address? [*]						
Cost of vaccine	--	57%	39%	50%	10%	31%
Would address no barriers	43%	3%	--	20%	43%	22%
Parent forgets	23%	10%	10%	13%	7%	13%

Country	Argentina (n=30)	Malaysia (n=30)	South Africa (n=31)	South Korea (n=30)	Spain (n=30)	Total (n=151)
Refused/Don't know	3%	13%	23%	--	23%	12%
Girls are in school or work during vaccination hours	--	3%	10%	10%	--	5%
Transportation	--	--	16%	--	3%	4%
Parents' work schedule	--	13%	3%	--	--	3%
Patient moves	--	--	16%	--	--	3%
Other [§]	13%	3%	19%	--	10%	11%
What advantages would a 2-dose HPV vaccine give your clinic [or school]? *						
Fewer appointments	43%	23%	39%	37%	83%	44%
Less need for recall	27%	10%	16%	17%	47%	23%
Less administrative costs for ordering, stocking, and monitoring HPV vaccine	13%	10%	29%	13%	33%	20%
No advantages	20%	50%	7%	20%	3%	20%
Better for patients	7%	3%	10%	17%	17%	11%
Refused/Don't know	13%	10%	10%	--	7%	8%
Less refrigerator space	--	--	16%	3%	7%	5%
Less workload/time	7%	--	13%	--	--	4%
Other ^{//}	--	--	--	13%	--	3%
What concerns do you have about a 2-dose HPV vaccine? *						
Vaccine efficacy	60%	70%	10%	77%	53%	54%
Vaccine safety	40%	33%	36%	17%	17%	29%
No concerns	20%	20%	26%	10%	23%	19%
Patient/parent forgets second dose	17%	--	--	--	27%	9%
Mistrust from parents	3%	--	16%	7%	--	5%
Other ^{**}	--	--	7%	3%	3%	3%
What would you need in order to not feel concerned about this anymore? *						
Information on efficacy	70%	80%	19%	87%	53%	61%
Information on safety	47%	60%	32%	50%	30%	43%
System to remind patients/parents about second dose	13%	--	--	--	20%	15%

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Country	Argentina (n=30)	Malaysia (n=30)	South Africa (n=31)	South Korea (n=30)	Spain (n=30)	Total (n=151)
Refused/Don't know	3%	3%	23%	--	13%	9%
List of talking points for discussion with parents	3%	3%	10%	--	3%	4%
Other ^{††}	3%	--	10%	3%	0%	3%

Abbreviations: HPV = human papillomavirus

* Totals may add up to more than 100%, multiple responses were accepted

[†] Missing (<3%) values were omitted from this table

[‡] Other includes: Depends on the evidence [n = 2 (Malaysia)]; 0 and 3 months [n = 1 (Argentina)]; 0 to 6 months is too much time [n = 2 (Spain)]

[§] Other includes: Time/number of office appointments [n = 2 (South Africa), n=1 (Malaysia)]; Shortage of stock [n = 2 (South Africa)]; Side effects/safety concerns [n = 1 (Spain), n=1 (Argentina)]; Long interval between doses [n = 2 (Argentina)]; Lack of follow-up [n = 1 (South Africa), n= 1 (Argentina)]; Achievable target [n = 1 (South Africa), n = 2 (Argentina)]

^{//} Other includes: Increased revenue [n = 3 (South Korea)]; Easier to explain/recommend to patients [n = 1 (South Korea)]

^{**} Other includes: Not enough stock available [n =2(South Africa)], Cost [n = 1 (Spain), n = 1 (South Korea)]

^{††} Other includes: Nothing [n = 3(South Africa), n = 1 (Argentina)], Better infrastructure [n = 1 (Argentina), n =1 (South Africa), n= 1(Spain), n = 1(Malaysia)]; Information, unspecified [n = 1 (South Africa), n = 1(Malaysia), n = 1(South Korea)]

Table 3:

Multivariable Correlates of 2-Dose Versus 3-Dose Preference Among Providers for the HPV Vaccine in the Multi-Site HPV Vaccine Acceptability Study (n=151)

	Proportion of 2-Dose Preference, %	Adjusted OR (95% CI) [*]
Country of Origin		
Argentina	80	Ref.
South Korea	90	2.25 (0.51, 9.99)
Malaysia	76	0.79 (0.23, 2.70)
South Africa	45	0.21 (0.07, 0.64)
Spain	83	1.25 (0.34, 4.64)
Type of Provider		
Ob/Gyno	76	Ref.
Nurse Practitioner/Other [†]	74	1.86 (0.51, 6.69)
Pediatrician	88	1.40 (0.36, 5.52)
Family medicine/General Practice	64	0.44 (0.13, 1.55)
Provider Years of Practice		
<17 years	75	Ref.
17 years	75	0.73 (0.32, 1.67)
Currently Provides the HPV Vaccine		
No	71	Ref.
Yes	76	0.63 (0.22, 1.81)
Provider's Average Number of Female Adolescents Seen per Month		
<20 patients	70	Ref.
20 patients	79	2.73 (1.04, 7.15)
Do you think a 2-dose HPV vaccination will be as effective as a 3-dose vaccine?		
No	59	Ref.
Yes	88	8.25 (3.09, 22.03)
Do you think a 2-dose HPV vaccine would have more or fewer side effects than the 3-dose?		
Fewer side-effects	79	Ref.
More side-effects	50	0.41 (0.02, 9.16)

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Proportion of 2-Dose Preference, %		Adjusted OR (95% CI) *
The same		0.57 (0.23, 1.41)

The same

73

0.57 (0.23, 1.41)

Abbreviations: HPV, human papillomavirus; OR, odds ratio; CI, confidence interval; Ref., referent group; Ob/Gyno: Obstetrician and/or gynecologist

* Adjusted models only include Country of Origin

† Other includes: Midwife (n = 9), Pharmacist (n = 2), Preventive Physician (n = 4),health promotion provider (unspecified) (n = 1), caregiver (n = 1)

Table 4.

Emergent qualitative themes related to 2-dose versus 3-dose HPV vaccination schedule from focus group discussions with mothers of vaccinated and unvaccinated daughters, stratified by country

Argentina	Malaysia	South Africa	South Korea	Spain
Support for 2-dose schedule	More convenient to complete Time saving for mothers Less burdensome on mothers and daughters	Willingness to follow government recommendations Confidence in researchers	More convenient to complete Timesaving for mothers Better “protection”	Favorable attitude towards scientific innovation More convenient to complete Belief that vaccine is new and improved
Barriers to 2-dose schedule				
	Less effective and less coverage Suspicion that 2-dose has not been adequately researched	Less effective and less “coverage” ^{*,*}	Less effective and less “coverage” ^{*,*} Suspicion that 2-dose has not been adequately researched	Suspicion that 2-dose has not been adequately researched Less effective and less “coverage” ^{*,*} Stronger concentration/ dose with 2 vs 3 doses, with potential for greater side effects/dose Acceptance contingent on safety and efficacy evidence
Other emergent themes	Suspicion of changing government recommendations Fear of change fueled by lack of knowledge Want more information from specialists	Number of doses less important than efficacy Favorable attitude towards scientific innovation	Positive association of vaccine price with efficacy Lower general knowledge on HPV and HPV vaccine Less concerned about side effects (relative to other FGDs)	Lower general knowledge on HPV and HPV vaccination Social stigma surrounds those who do not vaccinate More likely to request information on efficacy and safety before accepting 2-dose schedule

^{*} Mothers expressed concerns regarding longevity of HPV vaccine coverage with fewer doses.